A COMPARATIVE EVALUATION OF THIOPENTONE SODIUM AND PROPOFOL AS INDUCTION AGENT FOR CAESAREAN SECTION

THESIS

FOR

DOCTOR OF MEDICINE

(ANAESTHESIOLOGY)

BUNDELKHAND UNIVERSITY

JHANSI (U.P.)

2002 **RAJESH KUMAR**

CERTIFICATE

*This is to certify that the work entitled, "**A comparative Evaluation of Thiopentone sodium and Propofol as Induction Agent for caesarean section**" which is being submitted as a thesis for M.D. (Anaesthesiology) by **Dr. Rajesh Kumar** has been carried out in the Department of Anaesthesiology, M.L.B. Medical College, Jhansi.*

He has fulfilled the necessary stay in the department as required by the regulation of the Bundelkhand University, Jhansi.

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The technique embodied has been undertaken by the candidate himself and the observations have been periodically checked by me

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This piece of work

is dedicated

to my parents

ACKNOWLEDGEMENT

"O my God, to Him I pray

Increase my knowledge day by day"

After this little prayer to **God Almighty**, I extend my utmost, heart felt acknowledgement to my respected teacher, who embody vast knowledge and experience and perform the task of God by imparting knowledge to us and moulding our future.

It is a matter of great privilege to acknowledge my deepest sense of gratitude to my most revered teacher, **Dr. A.K. Gurwara**, (M.S., D.A.) Professor and Head of Department of anaesthesiology M.L.B., Medical College, Jhansi whose immense knowledge of the subject, analytic gaze and a great sense of precision has amassed fame to our department and institute. He has been a constant source of inspiration for me.

It is with a profound sense of Gratitude and regard that I express my thanks to **Dr. Pradeep Sahi**, (M.D., D.A.) Associate Professor, Department of Anaesthesiology, M.L.B. Medical College, Jhansi under whose able guidance and supervision I had the opportunity to carry out this work. His ever helpful nature, invaluable suggestions and most perceptive mind were a constant source of inspiration during the course of this work. The present work bears at every stage the impression of his keen interest. I shall forever be indebted to his for kindness and generosity. I am extremely grateful to **Dr. D.D. Verma** (M.D., D.A.) Professor, Department of Anaesthesiology, M.L.B. Medical College, Jhansi for his affectionate guidance, keen interest and constructive criticism extended to me during the period of this study.

I am deeply indebted to **Dr. (Mrs.) Veena Gupta** (M.D., D.A.) Associate Professor, Department of Anaesthesiology, M.L.B. Medical College, Jhansi for her helping attitude , expert guidance and supervision.

I am sincerely thankful to my friend, seniors and colleagues who were always ready to help me.

I am highly thankful to my wife Soni and beautiful daughter Rasu for their co-operation by giving time to me for completing my thesis.

I am very thankful to Mr. Zahir Hassan for typing the script of this text and for his assistance on many occasions in spite of personal inconvenience.

I am also thankful to Mr. Rafat J Siddiqui (Yes Computers, Sadar Bazar, Jhansi) for giving my thesis a final shape.

The debt I own to my parents Late Shri Shivnath and Smt. Shakuntla Devi is supreme for their silent, selfless support of my aspirations.

Last but not the least I thank the subject of this study, without whom cooperation this study could not be accomplished.

Rajesh Kumar

Date: 25-9-2001

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INTRODUCTION

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A women in labour posses one of the most critical of all problems to the anaesthetist. The anaesthetic care of the obstetric patient differs from that of her non-pregnant counterpart because of the physiological changes in the parturient, the presence of a second individual (the fetus) who is also affected by the anaesthetic process and the fact that the majority of request for anaesthesia are unplanned and urgent.

The success of anaesthesia in obstetrics depends largely upon surgical demand and materno-foetal well being. Hence the aim of anaesthesia is to provide safety and comfort to the mother, minimal neonatal depression and optimal working condition for the obstetrician.

The choice of anaesthetic technique between general and regional (epidural, spinal or combined epidural spinal) anaesthesia, which depends on patients preference to existing medical condition, the reason for surgery, the degree of urgency and the anaesthetist judgement and experience.

Regional anaesthesia is the most commonly employed technique as compared to general anaesthesia, as it is cost effective and has minimal incidence of aspiration. But regional anaesthesia is a time consuming procedure and does not allay anxiety and fear of this particular group of patient who are tired, anxious and exhausted and want to become unconscious as early as possible to avoid stress of surgery. Moreover there is a increased chance of hypotension which may produce serious foetal hypoxia affecting there by the neonatal out come.

General anaesthesia, the alternative technique for caesarean delivery overcomes the problems of regional anaesthesia. A good general anaesthesia is fundamental to the success and feasibility of obstetrical surgery practice. An ideal induction agent for caesarean delivery should be rapid and smooth acting, shorter in duration, devoid of cardiovascular and respiratory side effects and should be safe for both mother and foetus alike, should give good operating condition, as also devoid of post operative nausea and vomiting.

After introduction in 1934 by Water and Lundy, Thiopentone sodium because of its property of rapidly acting, act in one arm-brain circulation, producing peaceful sleep, gained rapid acceptance world wide and it remains to this day the commonest used induction agent for obstetric surgery. Although, Thiopentone sodium is quite safe but is not devoid of certain adverse effect like cardiovascular and respiratory depression, cough, sneeze, hiccup, pain and thrombophlebitis at the site of injection, nausea, vomiting, prolonged somnolence, psychic problem, motor disturbances, acute tolerance, true cutaneous allergy, anaphylaxis, laryngospasm, bronchospasm and neonatal depression.

After Thiopentone sodium many intravenous induction agent were introduced. These drugs lost their popularity because of their adverse effects :-

Propanadid, eugenol derivative, ultra short-acting non barbiturate is an oil base compound, causing hyperpnoea, tachycardia, cardiovascular depression or even cardiac arrest. Histamine release cause severe hypotension which lead to foetal hypoxia due to decrease in foetal blood flow. It can also causes allergic reaction and thrombophlebitis.

Althesin a mixture of two steroids (alphaxalone+alphadolone), causes tachycardia, hypotension, apnoea, muscle tremors, cough, hiccup and laryngospasm. The most important complication with its use is severe bronchospasm and circulatory collapse, an anaphylactoid reaction. Hypotension due to it can cause foetal hypoxia.

Etomidate, nonbarbiturate, an oil base compound, causes pain at site of injection, apnoea, increase in muscle tone and a high incidence of involuntary movement.

Diazepam, lipid-soluble benzodiazepine, is an oil base compound, causes venous irritation and thrombophlebitis. It causes slow onset of induction, rapidly crosses the placenta and with its metabolite nordiazepam produces prolonged effects including neonatal ventilatory depression, impaired thermoregulation, hypotonia and raised bilirubin serum concentration.

Midazolam, a water soluble benzodiazepine has slow onset of action, causes respiratory depression, prolonged sedation and more neonatal depression than ketamine and thiopental.

Ketamine causes increased skeletal muscle tone, with co-ordinated but seemingly purposeless movements, psychic emergence. Hypertension and tachycardia occur due to its sympathomimetic activity, causes uterine vasoconstriction leading to decrease foetal blood flow resulting foetal hypoxia.

Now presently Propofol, the most recent nonbarbiturate intravenous anaesthetic is introduced in to clinical practice by Kay and Rolly in 1977. They confirmed the potential of Propofol as an anaesthetic induction agent. Because of its rapid onset of action, short duration with rapid and clear headed emergence and lack of cumulative effect, Propofol has become very popular. It is also known to exert antiemetic action.

Since October 16, 1846 to the present day has been a long journey of more than one and half century. Scenerrio of intravenous anaesthesia is still changing because there is no ideal drug for induction of anaesthesia for caesarean section, presently, Thiopentone sodium is by now established as the induction agent of choice for caesarean section but work with Propofol for this purpose is still lacking. It is therefore worth while to study Propofol as an induction agent in obstetric practice particularly as far as safety of mother and neonate is concerned.

AIM OF STUDY

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1. To evaluate the efficacy of Propofol as an induction agent as compared to Thiopentone.

2. To assess maternal and foetal well being during Propofol induction against Thiopentone for caesarean sections.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

In the mid seventeenth century, soon after the description of the circulatory system by Harvey (1628), Percival Christopher Wren and Daniel Johan Major (1665) conceived the idea of injecting medicinal compounds directly in to the blood and performed the first experiment. Wren injected the opium solution in to the venous system of a dog by means of a quill fastened to bladder. The injection "stupefied" the dog with in a short time without killing it.

Pierre-Cyprian Ore (1872) is regarded as the true pioneer of intravenous anaesthesia. He used chloral hydrate intravenously to produce anaesthesia. But several unfortunate post operative deaths conspried against the acceptance of this method.

This followed another hiatus of 33 years. The process was started again by Krawkow (1905), who injected Hedonal (methyl-propyl-carbinal-urethane). Four years later Burkhardt popularised the intravenous use of Diethyl ether and Chloroform.

Neol and Souttar (1913) reported the use of intravenous paraldehyde followed by $MgSO_4$ (1916).

Nakagawa (1921) used Alcohol intravenously to induce surgical anaesthesia.

Barbituric acid was synthesized by Baeyer (1864), but its narcotic effect was not discovered. Later barbutric acid (Veronal) was synthesized by

Fischer and Vonmering (1903). Somnifaine was the first barbiturate to be given intravenously by Bardet (1924).

Father of intravenous anaesthesia, Helmeet Weese (1932) used Hexobarbitone. It was the first drug to make intravenous anaesthesia popular.

Sodium Pentothal, ultra short acting hypnotic synthesized by Ernest Henry Volwiler and Doralee Turben (1932) was first introduced into clinical practice by Lundy and Waters in1934. Although Lundy published the first report, but it is Waters to whom belongs the distinction of first clinical administration of Thiopentone in man. Its fate in the body and distribution was described by Brodie (1950). But unfortunately due to lack of an understanding of its pharmacokinetics, it was used in the same manner as diethyl ether and chloroform for the induction and maintenance of general anaesthesia and resulted in disasters including hypotension and prolonged sleeping times. It also lead to the casualties at Pearl Harbour resulting in so many deaths that intravenous Thiopentone was described as 'an ideal drug for "EUTHANASIA". An understanding of its pharmacokinetics and its desirable pharmacological properties made Thiopentone the standard anaesthetic drug to induce anaesthesia, but certain adverse effects like cardiovascular and respiratory depression, somnolence, psychic problems, motor disturbances, anaphylaxis,bronchospasm, cough, hiccup, nausea and risk with intra arterial injection mar its popularity as an ideal induction agent.

After Thiopentone sodium, many inducing agents were introduced with many side effects like Eugenol Derivatives (Propanadid) which is oil base compound causing increased incidence of phlebitis and release of

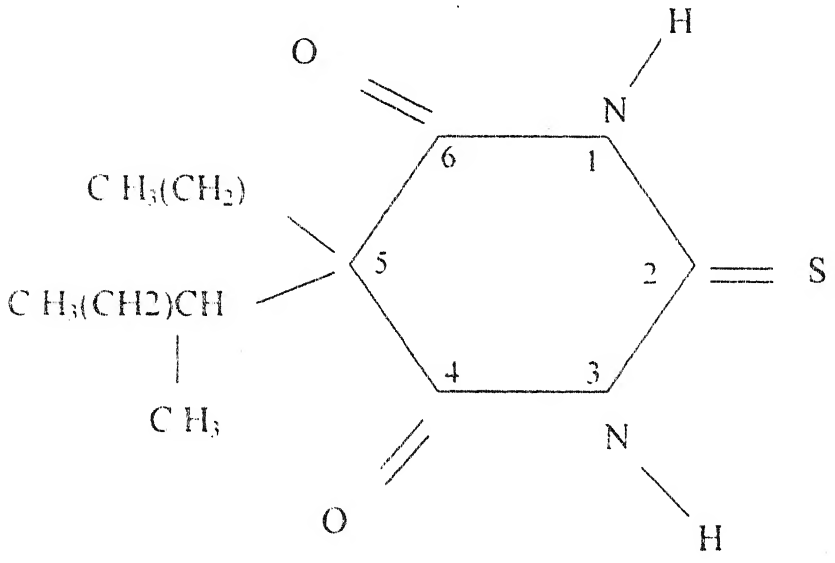
histamine causes allergic reaction, with Althesin anaphylactoid reaction, with Etomidate which is also oil base compound produces local pain, Diazpam also produces thrombophlebitis and with ketamine psychic emergence.

Propofol is the most recent intravenous anaesthetic was introduced into clinical practice by Kay and Rolly in 1977, who confirmed the potential of Propofol as an anaesthetic induction agent. Because of its rapid onset of action, short duration with rapid and clear-headed emergence and lack of cumulative effect, it reduces pressure on post operative facilities, with less incidence of nausea and vomiting in comparison to any other inducing agent.

A brief review of the pharmacokinetics and pharmacodynamics of Thiopentone and Propofol would therefore not be out of place before a discussion of there effect and utility as induction agents in clinical obstetric.

THIOPENTONE

Thiopentone is a derivative of barbituric acid (2-4, 6 trioxohexa hydro pyrimidine). It is an ultra short acting barbiturate. It differs from its predecessor pentobarbitone in having a sulphur atom rather than oxygen attached to one carbon atom resulting in more rapid induction and recovery.



5 ETHYL-5(1-METHYL – BUTYL) – 2-THIOBARBITURIC ACID

MECHANISM OF ACTION

Sedative hypnotic effect of Thiopentone is due to enhancement of action of GABA, while GABA mimetic effect i.e. directly activating chloride channel at slightly higher concentration may be responsible for barbiturate anaesthesia.

PHYSICAL PROPERTIES

The drug is used in the form of its sodium salt. Sodium Thiopentone is a pale yellow amorphous powder with a bitter taste and slightly sulphurous smell. Thiopentone is supplied in vials .25 g, .5 g or 1.0g. Thiopentone is a weak acid and its pKa is 7.60 and has optimal aqueous solubility at high pH values. At physiological pH, it is slightly more than half in the nonionised state. The commercial preparations contain sodium carbonate which prevent precipitation of the free acid by atmospheric CO_2 and results in an alkaline solution (pH – 10.5 – 11.0), solution is made 2.5% and it is stable for 1 week if refrigerated.

Hypnotic activity is introduced into barbituric acid molecule by the addition of side chains, especially if at least one of them is branched in position 5. The length of the side chain in the 5 position influences both the potency and duration of action of the barbituric acid derivatives. Replacing the oxygen atom with a sulphur atom at position 2 of an active barbiturate produces a barbiturate, with a more rapid onset and a shorter duration of action :- the thiobarbiturates. Methylation of an active barbiturate in position increases incidence of excitatory side effects.

Thiopental exists in 2 type of isomer (l) and (d) because of presence of asymmetric carbon atoms in one of the side chains attached to carbon 5 of the barbiturate ring. The (l) isomer is nearly twice as potent as the (d) isomers despite their similar access to the central nervous system.

PHARMACOKINETICS :

When administered intravenously, on first circulation, much of the drug is taken up from the injected bolus by tissues of high blood flow particularly the central nervous system and vital organs kidney, liver. The rate of drug transfer is very fast because of Thiopentone's lipophilic property and this correlates with it's rapid onset of anaesthetic action. Peak level in vessel rich tissue is reached in 1-2 min, because of its high solubility (partition coefficient) it diffuses rapidly into brain and subsequent slower transfer of the drug from the plasma occurs to other tissues which are less well perfused, first to muscle and later to fat depots. Such that plasma drug concentrations fall markedly and quickly, equilibrium with the muscle does not occur for about 15 min after administration. Although Thiopentone sodium is lipid soluble but because of poor vascularity of fat, concentration of drug increases in fat lately over about 2 hours. As the drug leaves the CNS for the periphery, recovery of consciousness ensues. At this time, most of the injected drug dose is still present in the body, nearly redistributed to the tissues. Eventually, sequestration occurs to fat depots, where the drug remains for many days in equilibrium with the relatively minute quantity in the plasma.

In the plasma, Thiopentone is bound with protein, predominantly albumin, to a normal extent of 70-80%. At high concentration of drug, the proportion bound is markedly reduced.

This binding limits the concentration of Thiopentone in free solution which is readily available for transfer to the brain in old age and in severe liver disease or malnutrition, where protein binding is impaired due to

hypo-proteinemia. More drug is available for transfer and an exaggerated anaesthetic response may result. In such circumstances, Thiopentone should be given in appropriately smaller dose. Drug which binds with proteins potentiate the effect of Thiopentone. Thus sulphafurazole and probenecid both exaggerate the response to standard dose of Thiopentone.

Thiopentone is eliminated almost entirely after metabolic degradation in the liver, less than 0.5 percent being excreted unchanged in the urine. Hepatic extraction ratio is 0.1 – 0.2. Metabolism renders, the molecule less lipid and more water soluble, thus depriving it the biological activity and redering it less readily reabsorbed in the renal tubules. The pathways involved in the liver is three fold

1. Side – chain oxidation at C_5
2. Oxidation replacement of sulphur at C_2 to form a small quantity of the drug's oxy equivalent, Pentobarbitone.
3. Ring clevage to form urea and a three carbon fragment.

Hepatic dysfunction slows elimination and can prolong recovery, though only after large doses.

The rate at which distribution and elimination occurs into three exponentials which represent distribution to high blood flow area (α1) distribution to low blood flow areas such a fat (α 2) and elimination (β). Thus half lives in young healthy patients with in the ranges

α_1 - 1.7 to 6.5 min.

α_2 - 23 to 71 min.

β - 5 to 10 hrs.

True drug elimination is therefore very slow, a total body clearance is high (82 - 288 ml/min) indicating that the reason underlying slow elimination is the large distribution volume which makes most of the drug inaccessible to the liver for its breakdown.

There are two important practical consequences of the prolonged elimination of Thiopentione :

(1) The residual effects of even a small single dose will persist for many hours, reducing mental anxiety and having an additive effect with other sedatives.

(2) The use of repeated small doses or infusion results in cumulation in adipose tissues and persistent effects for many days.

The usual induction dose is 4-5 mg/kg. for healthy adults.

Interpatient variability in the dose requirement for female can be calculated by formula :-

Dose (mg) = 300 + weight – 2 x Age -50

FACTORS INFLUENCING PHARMACOKINETICS

Pregnancy : Pregnancy has little influence on the pharmacokinetics of Thiopentone and although the clearance is greater in pregnant patients, the elimination half-life is longer. The drug diffuses freely across the placental barrier but the rapid redistribution in the maternal tissues between induction of anaesthesia and delivery is a major factor in producing a more alert baby than the mother's state would suggest. Certainly the umbilical venous plasma concentrations, which should be similar to those entering the fetal

brain, were well below the arterial plasma concentrations required to produce anaesthesia in adults.

Obesity *:* Patient have greater volume of distribution so longer terminal half time, also greater clearance but difference becomes insignifcant if values are normalised by body weight.

Rate of Administration *:* Slow injection rate are associated with a reduced incidence of apnoea and a significant decrease in arterial pressure. Rapid injection is associated with increased number of side effects.

Drug plasma protein binding *:* Hypoproteinemia in case of renal failure or malnutrition or due to any other cause results in reduced plasma binding of drug, so required induction dose is reduced. But clearance and elimination of the drug is unchanged in case of renal failure and affected only with very high doses in cirrhosis.

pH of Blood *:* Acidosis reduces the Thiopentone concentration in the plasma by up to 40%.

Age *:* Increasing age in associated with lower induction dose of Thiopentone because of lower cardiac output and failure to compensate for the effects of the drug on the circulation.

PHARMACODYNAMICS

1. Central Nervous System :

Thiopentone rapidly crosses the blood brain barrier and the concentration in the CSF, reaches a level almost as high as that of the unbound drug in the plasma. It causes sedation, hypnosis, anaesthesia and

respiratory depression like other barbiturates depending on the dose and rate of injection. There is an anticonvulsant action also. It produces progressive depression of the CNS. The cerebral cortex and ascending reticular activating system are depressed before the medullary centres. In clinical practice this is produced so rapidly that the classical signs of anaesthesia are of no value. Although respiratory depression is marked, patient with apnoea may yet react to a surgical stimulus.

Cerebral metabolic rate fall by about 50%, cerebral blood flow is reduced by 30-50%. In addition reduction in cardiac output and arterial blood pressure lead to secondary effects on cerebral perfusion. CSF pressure is also reduces. Thiopentone in dose insufficient to cause unconsciousness is antanalgesic and this sensitivity to pain lasts into the post operative period.

Acute tolerance: is seen with Thiopentone. There is a relationship between the induction dose of Thiopentone and the blood Thiopentone level at which patients awake from anaesthesia. The greater the induction dose, the greater will be the increments of drug required to maintain surgical anaesthesia. Because of acute tolerance it is difficult to correlate blood levels with depth of anaesthesia but about 7 µg/ml is an average level.

Return of normal mental faculties does not accompany apparent return of consciousness. Patient must not drive a car or engage in responsible activity for 24 hrs.

2) CARDIOVASCULAR SYSTEM :-

Under light anaesthesia, there is wide spread dilatation of the muscle and skin vessels but no obvious alteration in the total peripheral resistance. The increase in peripheral flow is compensated by constriction of the

splanchnic and renal blood vessels so that the blood pressure and cardiac output remains relatively unchanged.

In contrast, the rapid induction with bolus dose causes a reduction in arterial blood pressure, left ventricular stroke work index, pulmonary wedge pressure with marked peripheral vasodilatation. Peripheral vasodilatation causes pooling of blood in the extremities and reduction of the venous return to the heart leading to decrease in cardiac output. There is some degree of tachycardia (10-20%) which with lower doses contribute to maintenance of the blood pressure and cardiac output.

Higher doses of it causes increasing myocardial depression and vasodilatation but tolerable with normal cardiovascular system.

Dysrrhythmias occurs in a proportion of cases and are usually ventricular extrasystoles. The ability to compensate these changes is impaired in hypovolemic patients, so induction is hazardous in patients with compensated shock states. Also in patients with treated hypertension, heart can not compensate so Thiopentone induction may be dangerous. Patient with fixed cardiac output as with mitral stenosis, cardiac tamponade also required slow administration of the drug with careful assesment of anaesthetic depth.

3) RESPIRATORY SYSTEM :

Thiopentone in common with other barbiturates is a potent respiratory depressant, that it depress the spontaneous respiratory rate and depth and depress the sensitivity of the respiratory centre to CO_2. In deep anaesthesia with Thiopentone respiratory drive is maintained largely by the carotid sinus and is related to hypoxia. Depression of respiratory centre is antagonised by

surgical stimuli and potentiated by opioids, depending on the dose and rate of injection. The usual sequence of events when a dose of Thiopentone is given slowly is for a few deeper breaths to be taken just prior to the loss of conscionsness. There may be a brief period of apnoea due to direct effect of Thiopentone on respiratory centre coinciding with a low CO_2 tension from the preceding deep breaths. Respiration returns gradually and then further fade away as more Thiopentone is given.

During light anaesthesia, there is heightening of the laryngeal reflexes so that minor stimuli, local or remote may cause laryngospasm. If predisposing factor as sensitive bronchial tree in asthma or stimulation of the larynx by mucus is present, the patient may develop bronchospasm or laryngospasm but Thiopentone does not it self cause these conditions so it is preferable to avoid Thiopentone in asthmatic patient. Cough and hiccup are uncommon during induction with Thiopentone

4) **LIVER AND KIDNEY** :-

There is no evidence that Thiopentone adversely affects liver function unless hypoxia is present in conventional induction doses. There is transient impairment of liver function following large doses and infusions. Blood glucose concentrations are unaltered.

The effects of Thiopentone on the kidneys are secondary to its actions on the circulation. It causes liberation of antidiuretic hormone so that urine output during Thiopentone anaesthesia is decreased.

5) **ALIMENTARY SYSTEM** :-

Some depression of intestinal motility occurs but soon return to normal when patient is awake.

6) **EYES** :-

Pupils first dilate, then contract. Sensitivity to light remains until the patient is deep enough to permit incision of the skin and at this stages, the eyeballs are usually centrally placed. Intraocular pressure is reduced. Loss of eyelash reflex is a sign of induction of anaesthesia.

7) **REPRODUCTIVE SYSTEM** :-

In therapeutic doses, Thiopentone does not alter the tone of the gravid uterus or motility of the fallopian tubes. It rapidly crosses the placental barrier. Thiopentone is not harmful to the fetus when the drug is given for anaesthetic induction for caesarean in doses upto 6 mg/kg, but 8 mg/kg does depress the fetus. Placental circulatory factors and redistribution of Thiopental in the mother and fetus protect the fetal brain and spinal cord from high concentrations of barbiturates. Safe delivery of the fetus by caesarean section is possible if accomplished within 10 minutes after anaesthetic induction with Thiopentone.

8) **PORPHYRIA** :-

Porphyrin is a pigment formed in the liver from aminolaevulinic acid, a process catalysed by aminolaevulinic acid synthetase. Thiopentone stimulate aminolaevulinic acid synthetase enzyme so causing increasing in porphyria level which is already elevated in patient with porphyria. All types of porphyria are not adversely affected by Thiopentone but danger is so serious that Thiopentone is absolutely contraindicated in these patients. Thiopentone precipitates acute attack of porphyria.

9) **LOCAL EFFECTS :-**

Pain on injection and venous irritation are rare even when injected into small veins.

Venous thrombosis occur in about 3-4% cases. Rest to the affected part is the best treatment.

If injected subcutaneonsly in large volumes can cause tissue damage. Urticarial rash and anaphylactoid reaction can also occur.

The serious danger with Thiopentone is intra-arterial injection but reduced by the routine use of 2.5% solution.

Injection into artery lead to precipitation of crystals of insoluble Thiopentone and haemoglobin in the smaller vessels of the limb. ATP is then released leading to intimal damage and intravascular thrombosis Immediately on injection the patient complains of intense pain and radial pulse may disappear as arterial system undergoes generalised spasm due to release of noradrenaline. Avoidance is most readily achieved by awareness of danger and knowledge of aberrant arteries. Treatment includes leaving the needle or cannula in site, use of saline, lignocaine, papaverine in to the same vessel to encourage vasodilatation. Brachial plexus block can be performed to remove other vasoconstrictor influences.

Thiobarbiturates cause histamine release, but not by oxybarbiturate.

Thiopentone Sodium an Induction Agent in Obstetric Patients :-

In pregnancy there is a high cardiac output state, decrease in peripheral resistance, decrease in blood pressure and increase blood flow to the uterus. And also increase in blood volume and decrease in plasma protein but increase in total amount. These physiological changes of pregnancy lead to rapid onset of action of Thiopentone, less hypotensive effect, increased drug binding, less drug is required for induction as compare to non pregnant and slow elimination from the body although the clearance is greater therefore prolong somnolence. Rapid redistribution in the maternal tissue between induction of anaesthesia and delivery is a major factor in producing a more alert body than the mother state would suggest certainly the umbilical venous plasma concentrations which should be similar to those entering the fetal brain, were well below the arterial plasma concentration required to produce anaesthesia in adults. Thiopentone, being highly lipid soluble, crosses the placenta readily, but frequently does not have the expected profound effects in the neonate that might be expected because of the short interval between its administration for induction of anaesthesia and delivery of the infant. But in large dose (8mg/kg) does depress the fetus, and is not harmful to foetus when the drug is given for anaesthetic induction for caesarean section in doses up to 6mg/kg Thiopentone cause less awareness and due to its slow elimination from body prolong somnolence occur.

CONTRAINDICATIONS :

(1) ABSOLUTE : i) Prophyria – Not all type of porphyria, but danger is so great that risk can not be taken.
It causes precipitation of acute attack.

ii) Patient with history of Thiopentone anaphylaxis.

(2) RELATIVE : Special care is needed in these cases –

(a) Shocked, debilitated, severely anaemic and uraemia cases small dose are required.

(b) Patients with gross dyspnoea due to cardiac and respiratory disease, in fixed cardiac output disease.

(c) patients with respiratory obstruction or status asthmatic.

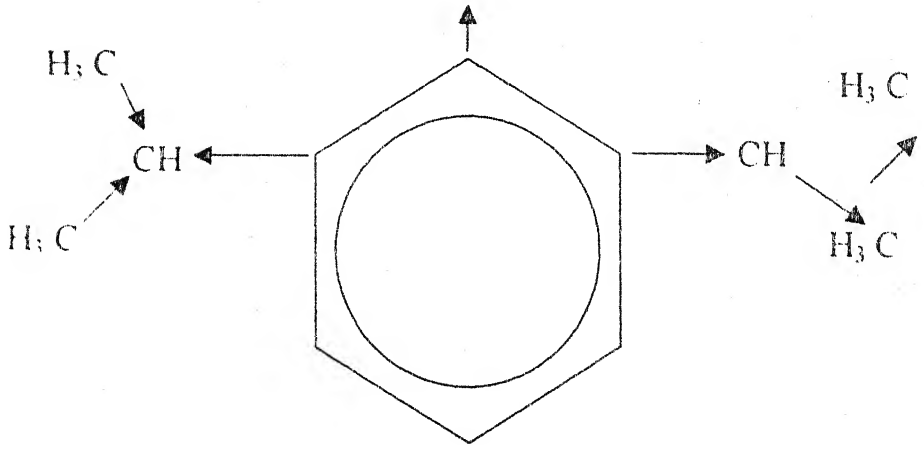
(d) Patient with difficult veins

PROPOFOL

Propofol (Diprivan) is the most recent intravenous anaesthetic to be introduced into clinical practice by Kay and Rolly in 1977.

PHYSICOCHEMICAL CHARACTERISTICS

Propofol is 2, 6- di–iso–propyl–phenol. It is one of a group of alkyl-phenols that have hypnotic properties. The alkyl-phenols are oils at room temperature and are insoluble in aqueous solution, but they are highly lipid soluble. The present formulation is in a 1 percent (wt/vol) emulsion of 10 percent soya bean oil, 1.2 percent purified egg phosphatide and 2.25 percent glycerol. This is similar to the fat emulsion Intralipid which is used for parenteral nutrition. Propofol has a pH of 7 and appears as a slightly viscous, milky white substance. Propofol is available as 1 percent solution in 10 ml and 20 ml vials. 20 ml clear glass ampules, 50 and 100 ml vials and in 50 ml prefilled syringes. It is stable at room temperature and is not light sensitive. If a dilute solution of Propofol is required, it is compatible with 5 percent dextrose in water.



PROPOFOL (2,6 di-iso Propyl-Phenol)

DOSAGE

The usual induction dose is 1.5 – 2.5 mg/kg

METABOLISM

Propofol is rapidly metabolised in the liver by conjugation to glucuronide and sulfate to produce water-soluble compounds, which are excreted by the kidneys. Less than 1 percent Propofol is excreted unchanged in urine, and only 2 percent is excreted in faeces. The metabolites of Propofol are thought not be active. Because clearance of Propofol exceeds hepatic blood flow, extra hepatic metabolism or extrarenal elimination has been suggested. Propofol itself results in a concentration dependent inhibition of cytochrome P-450 and thus may alter the metabolism of drugs dependent on this enzyme system.

PHARMACOKINETICS

Propofol is 98 percent protein bound and, being highly lipophilic, is distributed rapidly throughout the blood and vessel rich tissues. Blood level then decline with the initial distribution half life of 2 to 8 minutes and elimination half life has varied from 1.0 to 3 hours. Other worker have identified three compartment model of initial and slow distribution half lives of 1 to 8 minutes and 30 to 70 minutes and an elimination half life of 4 to 23.5 hours. The clearance of Protocol is extremely high – 1.5 to 2.2 L/min. which accounts for the rapid wakening from anaesthesia.

The pharmacokinetics of Propofol may be altered by a variety of factors (e.g. gender, weight, pre existing disease, age and concomitant medication). Propofol may alter its own clearance by decreasing hepatic

blood flow. Fentanyl reduces the clearance to approximately 1.3 L/min, by reducing Propofol distribution and increasing blood level. Propofol kinetics are unaltered by renal disease.

PHARMACOLOGY

EFFECT ON THE CENTRAL NERVOUS SYSTEM

Propofol is primarily a hypnotic. It acts by promoting the function of the β_1 subunit of GABA through activation of the chloride channel and thereby enhancing inhibitory synaptic transmission. It also inhibit the NMDA sub type of glutamide receptor through modulation of channel gating.

Propofol is not antianalgesic.

The onset of hypnosis following doses of 2.5 mg/kg is rapid (one arm brain circulation), with a peak effect seen at 90 to 100 seconds. ED_{50} of Propofol is 1 to 1.5 mg/kg following a bolus. The duration of hypnosis is dose dependent, being 5 to 10 minutes following 2 to 2.5 mg/kg.

In subhypnotic doses, Propofol provides sedation and amnesia. Propofol tends to produce a general state of well being. Recovery after Propofol 2.5 mg/kg is significantly faster. Propofol has a direct anticonvulsant effect which is dose dependent. Tolerance has been developed to Propofol following either repeat anaesthesia or prolonged infusion (days).

Propofol decreases intracranial pressure (ICP) in patient with normal or increased intracranial pressure. Normal cerebral reactivity to CO_2 and

autoregulation are maintained during a Propofol infusion. Propofol reduces cerebral metabolic rate of oxygen consumption ($CMRO_2$) by 36 percent. It also provide cerebral protective effects following an acute ischaemic insult.

EFFECT ON THE RESPIRATORY SYSTEM

Propofol is a potent respiratory depressant similar to barbiturates. Apnea occurs after an induction dose of Propofol; the incidence and duration of apnea appear to be dependent on dose, speed of injection and concomitant premedication. The onset of apnea is usually preceded by marked tidal volume reduction and tachypnea. Following induction dose it decreases respiratory rate significantly for 2 minutes and minute volume is significantly reduced for up-to 4 minutes.

The ventilatory response to CO_2 is also decreased during a maintenance infusion of Propofol. Propofol (1.5 – 2.5 mg./kg), results in an acute (13 – 22%) rise in $Paco_2$ & decrease in pH. Propofol (50 – 120 mg/kg/min) also depress the ventilatory response to hypoxia.

Propofol induces bronchodilation in patients with chronic obstructive pulmonary disease.

EFFECT ON THE CARDIOVASCULAR SYSTEM

The most prominent effect of Propofol is a decrease in arterial blood pressure during induction of anaesthesia. Independently of the presence of cardiovascular disease an induction dose of 2-2.5 mg/kg produces a 25 – 40 percent reduction of systolic blood pressure. Similar changes are seen in mean and diastolic blood pressure. The decrease in arterial pressure is associated with a decrease in cardiac output/cardiac index (≈15%), stroke

volume index (≈20%) and systemic vascular resistance (15 –25%). Left ventricular stroke work index is also decreased (by ≈ 30%). The decrease in systemic pressure following an induction dose of Propofol appears to be due to both vasodilation and myocardial depression. Both the myocardial depressant effect and the vasodilation appear to be dose dependent and plasma concentration dependent. The vasodilatory effect of Propofol appears to be due both to a reduction in sympathetic activity and to a direct effect on intracellular smooth muscle calcium mobilization.

Heart rate does not change significantly after an induction dose of Propofol. As Propofol either resets or inhibits the baroreflex, thus reducing the tachycardia in response to hypotension. Propofol has no direct effect on sinoatrial node function or on normal atrioventricular and accessory pathway conduction.

Heart rate may increase, decrease or remain unchanged when anaesthesia is maintained with Propofol. As the vasodilatory and myocardial depressant effects are concentration dependent, the decrease in BP from Propofol during the infusion phase is much less than that seen following an induction bolus. An infusion of Propofol results in a significant reduction in both myocardial blood flow and myocardial oxygen consumption therefore the global myocardial O_2 supply/demand ratio is preserved.

OTHER EFFECTS

Propofol does not potentiate neuromuscular blockade produced by both nondepolarizing and depolarising neuromuscular blocking agents. Propofol produces no effect on the evoked electromyogram or twitch tension; however, good intubating conditions after Propofol alone have been

reported. Propofol does not trigger malignant hyperpyrexia and is the anaesthetic of choice in patients with this condition.

Propofol following a single dose or a prolonged infusion does not affect corticosteroid synthesis or alter the normal response to ACTH stimulation. Propofol in the emulsion formulation does not alter hepatic, hematologic, or fibrinolytic function.

Propofol also possess significant antiemetic activity at low doses. Propofol at subhypnotic doses has also relieved cholestatic pruritus and was effective as naloxone in treating pruritus induced by spinal opiates.

Propofol cause a dose dependent decrease in the thermoregulatory threshold for vasoconstriction, but it has little effect on the sweating threshold.

Propofol only decreases polymorphonuclear leukocyte chemotaxis but not adherence phagocytosis and killing.

Propofol, an Induction agent in obstetric patients :-

Propofol is highly lipid soluble, has rapid onset of action, readily crosses the placenta and can cause foetal depression but is safe for foetus if induction to delivery time is less than 10 minutes. The clearance of it is extremely high. Therefore recovery from anaesthesia is rapid with clear headed emergence. It causes decrease in arterial blood pressure cardiac output/cardiac index, stroke volume index and systemic vascular resistance during induction leading to maternal hypotension so can lead to foetal hypoxia but these effects are less because of physiological change during pregnancy that is increase cardiac out put increase in blood volume and

increase in total body water compensates the hypotensive effect of Propofol. Propofol has antiemetic effect so very less chance of post operative nausea and vomiting. Propofol causes awareness during induction.

SIDE EFFECTS

Pain on injection can be found with administration of Propofol It is reduced by using a large vein, avoiding veins in the dorsum of hand, adding lidocaine to the Propofol solution and giving along with 5% Dextrose infusion.

Myoclonus can occur alter induction with Propofol. Apnoea following induction with Propofol is common.

Decrease in systemic blood pressure, is the most significant side effect on induction with Propofol.

Slow administration and lower doses in adequately prehydrated patients may attenuate the decrease in arterial pressure.

1. Kosaka Y., et al (1969) studied the intravenous thiopental anaesthesia for caesarean section, they concluded that Thiopentone is not harmful to the fetus when the drug is given for anaesthesia induction for caesarean section in doses up to 6 mg/kg, but 8 mg/kg does depress the fetus.

2. Hulton et al (1978) evaluated that Methohexitone and low dose ketamine appear to offer reasonable alternative to Thiopentone for anaesthetic induction at caesarean section.

3. Denis J. Morgan, et al (1981) studied the pharmacokinetics and plasma binding of thiopental in pregnant women going for caesarean section. They concluded that apparent volume of distribution, volume of distribution at steady state and elimination, half life are significantly greater at caesarean section and that systemic plasma clearance show a similar trend as comparison with non pregnant patient receiving Thiopentone for induction. They demonstrated that difference in maternal distribution and elimination characteristics of Thiopentone may be more important determinants of inter subject differences in fetal drug exposure than difference in dose or elimination half life.

4. Bernstein K. et al (1985) studied the influence of two different anaesthetic agents on the newborn and the correlation between foetal oxygenation and induction delivery time in elective caesarean section. They concluded that safe delivery of the fetus by caesarean section is possible if accomplished within 10 minutes after anaesthetic induction with either thiopental or Ketamine.

5. Gaspari F. et al (1985) studied the elimination kinetics of Thiopentone in mothers and their newborn infants. He resulted that at delivery, 4-9 min after induction, drug concentrations in cord blood were half those in maternal blood. The mean half – life of Thiopentone in the first renal clearance of Thiopentone was estimated in the newborn ; 0.074 ml/h/kg. Only 0.0007% (about 2 micrograms) of the maternal dose was recovered in the urine of newborn over 36h.

6. Schultetus R. R. et al (1985) used Ketamine (1 mg kg – 1) or Thiopentone (4 mg kg –1) to induce anaesthesia for caesarean section in 62 normotensive patients. During induction and before laryngoscopy, blood pressure did not change in either group, when laryngoscopy and intubation were performed mean blood pressure of both patient group increased 20-30 percent, with Ketamine heart rate was unchanged from pre-induction rate of 85 beats/min before laryngoscopy and increased significantly by 15 percent during laryngoscopy and intubation, with Thiopentone heart rate increased significantly to 20 percent during induction and increased further to 35 percent during laryngoscopy and intubation, Neonatal outcome was good and did not differ significantly between groups.

7. Bland B.A. et al (1987) administered 0.2 mg/kg Midazolam or Thiopental 3.5 mg/kg, with succinylcholine 1 mg/kg for rapid sequence induction in sixty healthy mothers undergoing elective caesarean section randomly. Maintenance of anaesthesia was identical in all patients. Haemodynamic responses were similar as were the biochemical status of mothers and infants. However 1 minute Apgar minus color (A-C) scores less than 5/8 (representing 'severe' neonatal depression) were recorded in five infants after midazolam so it is concluded that midazolam is less suitable than Thiopental for induction in patients undergoing caesarean section.

8. Baraka A. et al (1989) concluded that awareness was significantly greater induction with Thiopentone (70 percent) than after Ketamine (13.3%) in patients undergoing caesarean section.

There was no significant difference in Apgar scores or umbilical vein blood gas values in the new borns.

9. Bach V. et al (1989) studied placental transfer and elimination of Midazolam and Thiopentone in neonates delivered by mothers who were induced by Midazolam or Thiopentone. Placental transfer of Thiopentone (0.96) was significantly more rapid than the transfer of Midazolam (0.66) and Alpha – hydroxy Midazolam (0.28). elimination half – life in neonates was 6.3 hours for Midazolam and 14.7 hours for Thiopentone.

10. Celleno D. et at (1989) studied the neurobehavioural effects of Propofol on the neonate following elective caesarean section. Forty mothers undergoing elective caesarean section under general anaesthesia were allocated randomly to receive either propofol 2.8 mg kg-1 (n=20) or Thiopentone 5mg kg-1 (n=20). He found that infant in the Propofol group had lower Apgar scores at 1 and 5 min; 25% of them had muscular hypotonus at 5 min. this hypotonus was not noted during the early Neonatal Neurobehavioural scale (ENNS) examination. Newborn children examined 1 h after birth after maternal anaesthesia with Propofol, showed a depression in alert states, pin prick and placing reflexes, and mean decremental count in Moro and light. There was a generalized irritability in 25% of them. This depression was not observed at 4h.

11. Crowford M. E. et al (1989) compared Thiopentone and Midazolam induction in 40 women planned for caesarean section. They found no statistically significant difference in both groups at

induction during operation or recovery, in systolic blood pressure and heart rate. Vomiting was significantly more frequent after Thiopental. So Midazolam appears to be suitable alternative to Thiopental for induction and maintenance of anaesthesia.

12. Moore J. et al 1989, compared Propofol and Thiopentone as induction agents in obstetric anaesthesia. They found that blood pressure was lower in the Propofol group during the induction – delivery interval. Umbilical/maternal vein ratios for Thiopentone and Propofol were 8.5 and 7.2 respectively. Infant well being is judged by Apgar score and cord blood analysis showed little difference between the two induction agent. Factors associated with uterine relaxation and bleeding were similar in two groups.

13. Ravlo O. et at (1989) assessed the general condition of 40 neonates followingThiopental or Midazolam based general anaesthesia for elective caesarean section and concluded that Midazolam is as safe as Thiopentone.

14. Valtonen M. et al (1989) compared Propofol and Thiopental for induction of anaesthesia for elective caesarean section. He concluded that induction characteristics and hemodynamic response to Propofol and Thiopentone were similar. Side effects were rare with both agents, but Propofol caused more discomfort on injection compared to Thiopentone. Recovery times were shorter after Propofol as evaluated by time to orientation, recovery scoring after anaesthesia and measurement with the Maddox wing. Rapid placental transfer and significant fetal uptake were detected for Propofol. There was no significant neonatal depression as

assessed by Apgar scores & blood gas analysis. Propofol appears to be suitable alternative to Thiopentone as an induction agent for anaesthesia in elective caesarean section.

15. Gin T. et al (1990) studied the haemodynamic effects of Propofol and Thiopentone for induction in forty women for elective caesarean section. He concluded that post induction arterial pressures were similar to pre-induction values with no differences between Thiopentone and Propofol. Following intubation, the rise in systolic arterial pressure was greater in the Thiopentone group, 32.1 mm Hg (SD 23.7) compared with the Propofol group, 17.4 mm Hg (SD 23.8), $P< 0.05$). in the Thiopentone group, arterial pressures were slower in returning to baseline values. Heart rate initially elevated in both groups to the same degree. At caesarean section, induction with Propofol causes less variation in arterial pressure than Thiopentone. Hypotension is probably prevented by the coincident stimulus of rapid sequence induction. Neonatal Apgar scores were similar between the two groups.

16. Gin T. et al (1990) compared the pharmacokinetics of a bolus induction dose of Propofol 2 mg/kg in 10 women undergoing elective caesarean section with those in six non-pregnant women having laproscopic sterilization. Non compartmental analysis estimated that the women undergoing caesarean section had a similar elimination half life (mean 81.27 (SD 18.87} min) and apparent volume of distribution at steady state (2.66 {0.63} litre/kg) as non-obstetric patients (99.45 {29.40} min and 3.360 (1.87} litre/kg). Clearance was more rapid in the caesarean section

group (39.32 {8.07} ml/min/kg vs 29.40 {8.72} ml/min/kg) ($P< 0.05$).

17. Gin T. et al 1990 studied the maternal and fetal level of Propofol at caesarean section. Twenty women were given a bolus induction of Propofol 2.0mg kg-1 for caesarean section they found that at delivery the maternal venous (MV) concentration of Propofol ranged from 0.53 to 1.48 μg/ml, umbilical vein (UV) 0.39 to 1.4 mg/ml and umbilical artery (UA) 0.34 to 0.68 μg/ml. MV Propofol concentrations were always higher than corresponding UV concentrations. The mean UV/MV ratio was 0.65 (0.56-0.74) and the mean UA/UV ratio was 1.07 (0.99-1.15). Neither ratio was shown to be correlated with induction to delivery time. Distribution of Propofol is rapid across the placenta and in the fetus. Apgar scores higher with shorter incision to delivery times but were not correlated to umbilical level of Propofol.

18. Gregory MA. et al (1990) studied the Propofol infusion anaesthesia for caesarean section. After induction of anaesthesia with Propofol 2 mg/kg, ten pregnant women received Propofol 6 mg/kg/hr and nitrous oxide 50 percent in oxygen while ten were given Propofol 9 mg. Kg-1. hr-1 with 100 percent oxygen. The other ten pregnant women received Thiopentone 4 mg. Kg^{-1} and nitrous oxide 50 percent in oxygen with enflurane one percent. Haemodynamic changes were similar immediately following induction but the low Propofol infusion group had the best haemodynamic stability subseqnently. Recovery times were fastest in the low infusion group but there were no difference in later postbox testing.

Neonatal Apgar scores and umbilical blood gas analysis were similar but NACS at two hours were poorer in the high infusion group. A Propofol infusion coupled with nitrous oxide appears to be a satisfactory technique for Caesarean section.

19. Kanto J. et al (1990) studied the pharmacokinetics and pharmacodynamics of induction agent Propofol in caesarean section. The induction properties and pharmacokinetics of Propofol, 2.5 mg/kg 1.v, were studied in twelve unpremedicated healthy pregnant patients at term. The onset of anaesthesia was rapid (27.7 + 1-7.3 sec) and the quality of induction, maintenance of and rapid recovery from anaesthesia were clinically very acceptable. On the basis of Apgar scores and blood gas analyses of the feto-placental unit, Propofol appears to be a safe alternative to other available induction agents. The pharmacokinetics of Propofol in pregnant women were described by a high value for total body clearance (mean 2189.6 ml/min) and a short elimination half-life (mean 24.1 min)

20. Gin T. et al (1991) compared the pharmacokinetics of a bolus dose of Propofol 2 mg kg-1 in eight patients undergoing caesarean section with those in eight postpartum patients undergoing sterilization by mini-laprotomy. Caesarean section group had a total body clearance of (medium) 31.5 (range 24.4-6.61) ml min-1 kg –1, apparent volume of distribution at steady state 5.10 (2.46-6.61) litre kg-1 and mean residence time 1.61 (52.3-251) min : volume for postpartum groups were 33.8 (21.5-47.2) ml min-1 kg-1, 5.17 (3.47-8.09) litre kg-1 and 163 (92.3-23.8) min respectively.

The 95% confidence interval for the unbound Propofol in maternal venous ratio of Propofol at delivery was 0.62-0.86 Plasma protein binding studies showed there was less unbound Propofol in maternal plasma (1.28-2.29%) compared with umbilical plasma (2.08-3.88%) ($p<0.01$). Neonatal concentrations of Propofol were greater than maternal concentrations at 2 hours.

21. Yau G. et al (1991) studied the Propofol for induction and maintenance of anaesthesias at caesarean section in a comparison with Thiopentone/enflurane. Twenty patients received Propofol 2mg/kg for induction of anaesthesia followed by Propofol 6mg/kg/hour, while twenty patients received Thiopentone 4 mg/kg with enflurane 1% for maintenance of anaesthesia. The hypertensive response after intubation was of shorter duration in the Propofol group compared with the Thiopentone group. Induction to delivery times ranged from 5 to 14 minutes and neonates from both groups had similar and satisfactory Apgar scores. Neurologic and Adaptive capacity scores and umbilical cord blood gas analysis. However, a prolonged Propofol infusion time before delivery may cause lower neurologic and adaptive capacity scores. There were no differences in maternal recovery times or psychomotor performance.

22. Siafaka I. it al (1992) compared Propofol and thiopental as induction agents for elective caesarean section. He found that there were no significant differences in haemodynamic response between the two groups, during intubation heart rate rose in both groups, but remained increased five minutes after tracheal intubation only in

the thiopental treated woman (P< 0.05). there were no significant monatal depression as assessed by Apgar scores & blood gas analysis. Propofol appears to be a suitable alternative to thiopental as an induction agent for obstetric anaesthesia.

23. Audibert G.B, et al (1993) studied the concentration of Propofol in maternal and fetal blood during anaesthesia for caesarean section. Ten patients were studied in which anaesthesia was induced and maintained with Propofol (2mg/kg in 15 seconds; 3 mg/kg/h until the end of the operation). A series of maternal blood samples have been obtained at delivery. The results (measured by high pressure liquid chromatography) were : at delivery the mean ratio of the drug concentration in the umbilical vein to that in maternal vein was 0.53 $\pm$ 0.16 mg/ml : the mean concentration in the umbilical vein was 0.96 $\pm$ 0.31 mg/ml. The anaesthesiogical protocol was clinically satisfactory and had no adverse effects on mother and foetus.

24. Celleno D, et al (1993) compared the thiopental sodium, Propofol and midazolam for induction of anaesthesias in patients undergoing elective caesarean section. Three groups of 30 patient each receiving thiopental 5 mg/kg, Propofol 2.4 mg /kg or midazolam 0.3 mg/kg for induction of anaesthesia. He found that in the thiopental and midazolam groups, systolic blood pressure and heart rate rise following endotracheal intubation and skin incision ($p < 0.001$ and $p < 0.0025$, respectively), while in the Propofol group, there was significant hypotension after induction ($p < 0.005$) electroencephalographic patterns showed a light depth of

anaesthesia with Propofol and midazolam between anaesthesia induction and delivery, confirmed by the presence of clinical signs of light anaesthesia in 50% of Propofol patients and 43% of midazolam patients. Time to induce anaesthesia was longer with midazolam ($p < 000001$). Neonates in the midazolam and Propofol groups had lower Apgar and neurobehavioural scores than those in the thiopental group. Umbilical artery to umbitical vein ratio were above 1 in the Propofol and midazolam groups.

25. Gin T, et al (1993) studied the plasma catecholamines and neonatal condition after induction of anaesthesia with Propofol or Thiopentone at caesarean section. They found that the increase from baseline values in mean arterial pressure after tracheal intubation was greater in the Thiopentone group [29 (SD 15) mm Hg] compared with the Propofol group [18 (14) mm Hg) ($p < 0.01$)]. The concentrations of noradrenaline and adrenaline increased in both group after tracheal intubation. Maximum noradrenaline concentration were greater in the Thiopentone group [413(177) pg/ml] compared with the Propofol group [333(108) pg/ml] ($P< 0.05$), but there were no differences between groups in adrenaline concentrations. Neonatal Apgar scores, neuro-behavioural testing and umbilical catecholamine, blood gas tension and oxygen content analysis were similar between groups. Propofol attenuated the hypertensive and catecholamine response associated with laryngoscopy and tracheal intubation but there was no improvement in neonatal out come.

26. Sariev A.K. et al (1993) studied the pharmacokinetics and pharmacodynamics of thiopental sodium in pregnant women during caesarean section Group I consist of 6 women (Thiopental dose 8.0 mg/kg was combined with components of neuroleptanalgesia), group II consisted of 7 women (The drug dose 4.68 mg/kg was combined with moradol analgesia). The higher Apgar score was characteristic of the newborns from group II was due to the potentiating effect of moradol. In both groups a correlation has been established between pharmacokinetic parameter and haemodynamic changes, as well as between sodium thiopental concentration in maternal and umbilical blood and pharmacokinetic parameters.

27. Teviotdale B.M. et al (1993) studied the Veuronium-Thiopentone induction for emergency caesarean section under general anaesthesia. In this series of thirty cases vecuronium 8 mg preceding Thiopentone 250mg and atropine 0.6mg by 20 seconds provided effective induction and easy intubating conditions with out clinical effects on the newborn maternal acid aspiration, or clinical signs of persistent paralysis after reversal.

28. Zamora E. et al (1994) studied the effects on the newborn infant of thiopental and Propofol used in anaesthetic induction in caesarean section. Anaesthesia was induced with thiopental 4 mg/kg in one group; in the other group, Propofol 2mg/kg was used. He concluded that if the induction extraction interval is 10 min or less, both thiopental (4 mg/kg) and Propofol (2 mg/kg) given in a single

dose for induction of general anaesthesia in all types of caesarean section are equally safe for the new born infant.

29. Kee W.D. et al (1997) studied the post operative analgesic requirement after caesarean section : a comparison of anaesthetic induction with ketamine or thiopental. He compared postoperative pain and analgesic requirement in patients who underwent elective caesarean section under general anaesthesia induced with thiopental 4mg/kg or ketamine 1mg/kg. Anaesthesia was maintained with nitrous oxide and isoflurane. Post operative analgesia was provided by Patient Control Analgesia (PCA) using morphine. He concluded that induction of anaesthesia for caesarean section using ketamine is associated with a lower postoperative analgesic requirement compared with thiopental. Ketamine unlike thiopental has analgesic properties that may reduce sensitisation of pain pathways and extend in to the postoperative period.

30. Djordjevic B. et al (1998) compared propofol and Thiopentone as induction agent for elective caesarean section. A total of 40 female patients were randomly divided in two equal groups each of them was to receive different anaesthetic : Propofol 2.5 mg/kg (n=20) or Thiopentone 5mg/kg (n=20. they concluded that following induction of anaesthesia a significantly greater decrease of blood pressure and heart rate was found in the Propofol group, when compared with the patients in Thiopentone group. During the induction and maintenance of anaesthesia, the frequency of adverse effects was greater in Thiopentone, than in Propofol group (6/20 versus 2/20 patient). There was no significant difference between

the groups when induction-delivery interval was concerned. The new-borns from the propofol group had significantly higher Apgar score in the 1st minute (8.35) and 5th minutes (9.25), than the new-borns in Thiopentone group (7.90) and 8.90, respectively).

31. Sanchez-Alcaraz A. et al 1998 studied the Placental transfer and neonatal effect of Propofol in caesarean section. Intravenous Propofol was administered as an anaesthesia – inducing agent at doses of 2 mg kg-1 in ten healthy pregnant women (ASA I-II). They concluded that Propofol plasma levels in the newborn at the time of delivery depend on the level in maternal plasma, and therefore on the dose used for induction and the time lapsed between the administration of the drug and the delivery of the foetus.

32. Kotur P.F. et al (2000) compared the injection Propofol and injection Thiopentone as induction agents in anaesthesia for caesarean section. He resulted that induction characteristics were comparable in both groups. Induction time and time for recovery were faster in Propofol group when compared with Thiopentone group. There were clinically acceptable haemodynamic changes in both groups and Apgar scores at 1 mm and 5 min were comparable between two groups. Incidence of complications were nil in both groups except involuntary muscle movement in five patients during induction in Propofol group.

MATERIAL AND METHODS

MATERIAL AND METHODS

The present study was conducted on 90 young pregnant patients of ASA grade I and II, scheduled for elective caesarean section under general anaesthesia, admitted in the department of Gynaecology and Obstetrics, M.L.B. Medical college and Hospital, Jhansi.

Criteria for including the patients in the study are :

1. Patient with no antipartum haemorrhage.
2. Patient with no cardiac disease like valvular heart disease.
3. Patient with no foetal distress.
4. Patient with no pregnancy induced hypertension or eclampsia.
5. Patient with no full stomach.
6. Patient with no associated medical problems – like diabetes, liver disease etc.

Each selected patient was randomly assigned to one of the three following group, containing 30 patients each and depending on the induction agent used.

Group I - Thiopentone sodium 2.5% 5mg/kg body weight

Group II - Propofol 0.5% 2 mg/kg body weight

Group III - Propofol 1% 2 mg/kg body weight

Detailed clinical history was obtained from all selected patients regarding :-

1. Any disease of respiratory system, cardiovascular system, Hepato billiary system, renal and central nervous system present or past.
2. Any drug allergies.
3. Previous drug intake.
4. Course of present pregnancy
5. Course of previous pregnancies and complication thereof if any.
6. Any previous anaesthetic administration.
7. Any drug abuse or addiction or habituation.
8. Social and economic status.

They were then subjected to the following scheduled clinical examination.

General Examination :-

1. Pulse :- rate, rhythm, volume, character, and synchronicity with other side.
2. BP – Systolic and diastolic both.
3. Body weight in kg.
4. Temperature
5. Hydration of patients
6. Oral hygiene.

7. Anaemia

8. Icterus

9. Assessment of airway by adequate mouth opening and neck movement.

10. Edema.

11. Any spinal deformity like kyphosis, scoliosis etc.

Systemic Examination:-

Respiratory system - rate, rhythm, movement of chest, palpation, percussion and auscultation

Cardiovascular system - Inspection, palpation of the precordium and auscultation of heart sounds in all four cardiac areas-like mitral, tricuspid, aortic and pulmonary area.

Abdominal examination - Inspection and palpation for any fluid or organomegaly

C.N.S. examination:-

1. Sensory system - The sensation of touch, pain, temperature position, vibration and cortical senses were tested in all patients.

2. Motor System:-

(a) Superficial Reflexes - like planter and abdominal reflexses were tested in all patients.

(b) Deep tendon Reflexes- like biceps, triceps, knee jerk, ankle jerk were tested.

Patients were then investigated as follows :-

1. Blood examination - Hb% TLC, DLC, Sugar, Urea and Creatinine

2. Urine examination - a) Routine < Sugar / Albumin
   b) Microscopic

3. EKG in all leads

4. Chest X-Ray (PA view)

5. Special investigations as and when indicated.

Pre-medication:-

All patients were assured and reassured during pre-anaesthetic check up. Proposed technique of anaesthesia was explained to everyone in detail and a written and informed consent obtained. Patients were kept fasting for 8 to 12 hours prior to surgery. Injection Metoclopramide 0.2 mg/kg body weight and injection Ranitidine 1.0 mg kg-1 body weight were given intramuscularly 45min before induction of anaesthesia. Injection Atropine 15µg/kg body weight was given intravenously 5 minutes before induction of

anaesthesia inside the operation theatre through an I/V line preset using 5% Dextrose solution.

Induction:-

Preoxygenation was done with 100% oxygen for 3-5 minutes. Patients were induced by either Thiopentone sodium 5 mg kg-1 body weight (Group-I) or Propofol 2 mg kg-1 body weight 0.5% solution (by adding equal amount of 5% dextrose) (Group – II) or Propofol 1% (Group-III) through slow I/v injection over a period of 30 seconds. Ventilation was assisted with 100% of oxygen as and when apnoea occurred. Larynogoscopy was then performed under the effect of suxamethonium in doses of 1.5 mg kg-1 body weight and proper size endotrachial tube introduced atraumatically. Patients were then connected to Boyle's Basic Anaesthetic machine via Bain's rebreathing anaesthetic circuit and I.P.P.V started.

Maintenance:-

Anaesthesia was maintained with O_2 and N_2O in a ratio of 40:60 and Vecuronium bromide (non-depolarising muscle relaxant) and intermittent positive pressure ventilation.

Reversal:-

On completion of surgery residual neuro muscular block was reversed by Neostegmine (45 µg/kg body weight) and Atropine (25 µg/kg body weight) I/V slowly.

Observation:-

During induction following data were observed and recorded

1) Pain on injection

2) Induction time in seconds from injection to spontaneous closure or loss of eyelid reflex.

3) Pulse rate.

4) Blood pressure – Systolic and Diastolic, during induction during laryngoscopy and then at regular interval till the end of surgery.

5) Arterial Oxygen saturation.

6) Abnormal limb movements

7) Presence or absence of apnoea

8) Side effects if any like cough and hiccup.

9) Apgar scores

10) Post operatively patients were enquired about acceptance with particular reference to induction phase and any incidence of awareness during anaesthesia.

OBSERVATIONS

Table – 1

Distribution of Patients According to Age

Age Yrs	Number of Patients				
	Group I Thiopentone (2.5%)	Group II Propofol (0.5%)	Group III Propofol (1.0%)	Total	%age
16-20	3	2	4	9	10
21-25	16	13	14	43	47.77
26-30	10	12	10	32	35.55
31-35	1	3	2	6	6.66
>35	-	-	-	-	-
Total	**30**	**30**	**30**	**90**	**100.00**

Table I shows that maximum number of patient 43 (47.77%) belong to 21-25 years of age group.

DISTRIBUTION OF PATIENTS ACCORDING TO AGE

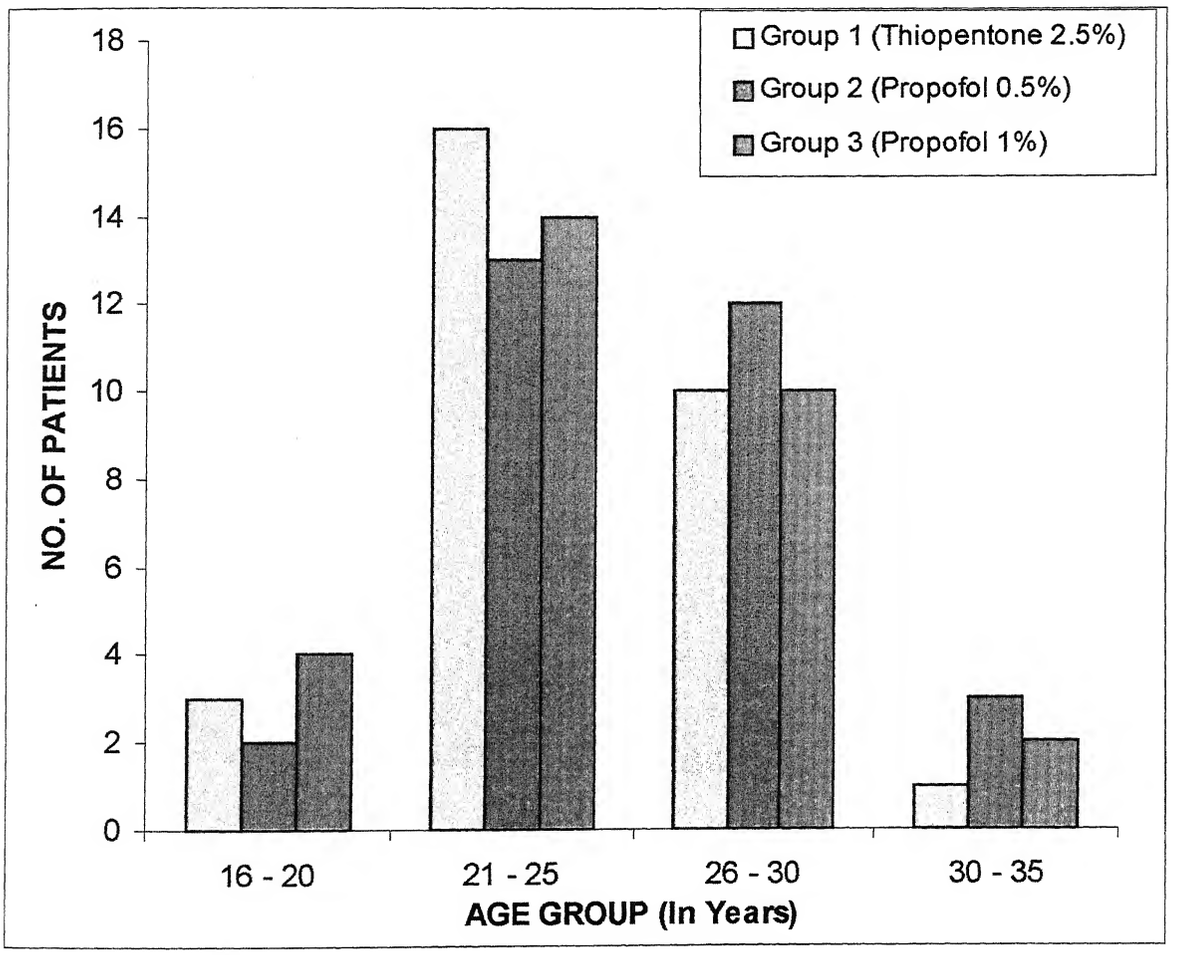


Table – II

Distribution of Patients According to Body Weight

Weight in kg	Number of Patients				
	Group I Thiopentone (2.5%)	Group II Propofol (0.5%)	Group III Propofol (1.0%)	Total	%age
41-50	10	12	11	33	36
51-60	15	14	16	45	50
61-70	5	4	3	12	13.33
>70	-	-	-	-	-
Total	**30**	**30**	**30**	**90**	**100.00**

Table II shows that maximum number of patient 45 (50%) were weight between 51-60 Kg. in all the three groups.

DISTRIBUTION OF PATIENTS ACCORDING TO BODY WEIGHT

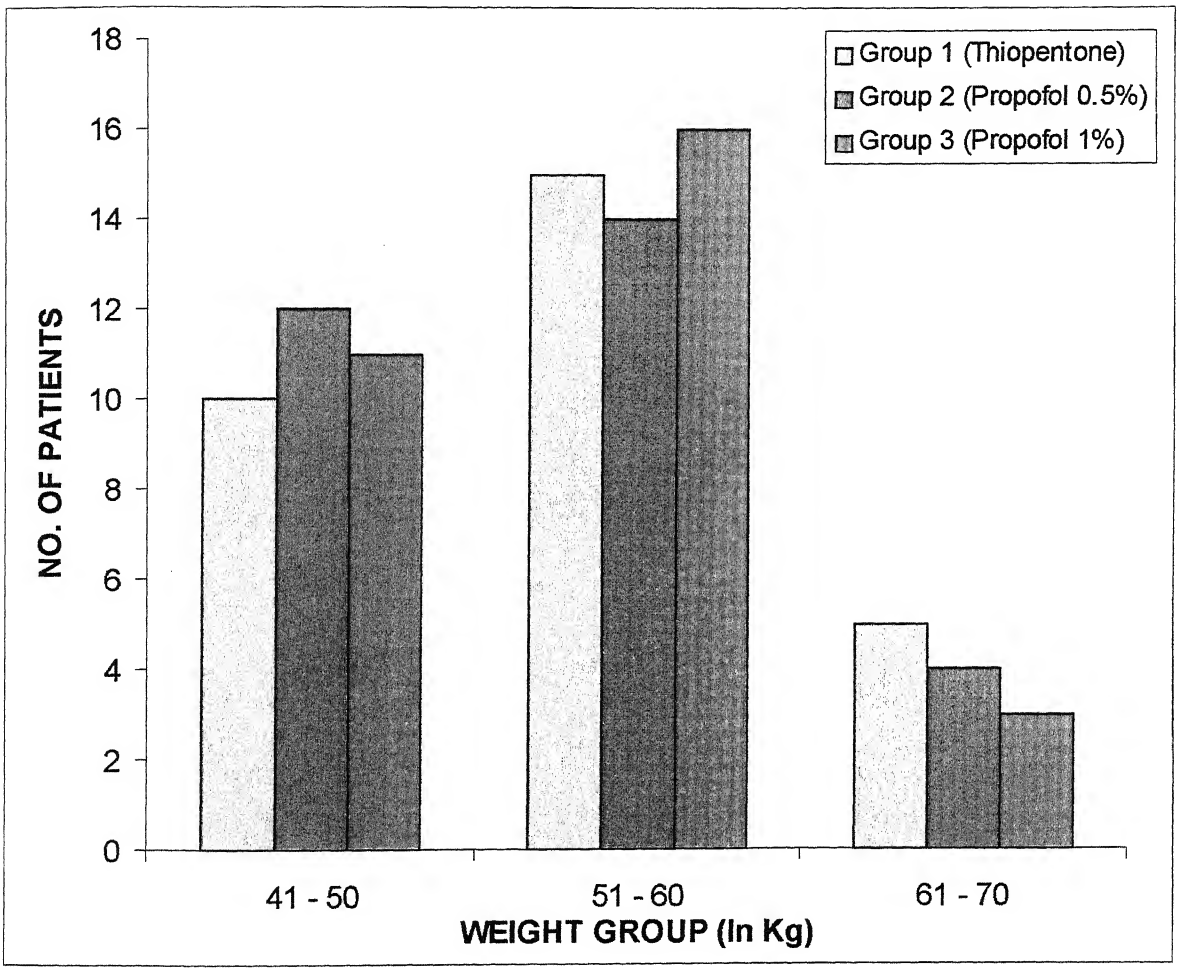


Table – III

Time for Onset of Induction (Seconds)

Time (Seconds)	Group I Thiopentone 2.5%)	Group II Propofol (0.5%)	Group III Propofol (1%)
Mean ± SD	47.20 ± 7.26	70.5± 19.58***	40.1 ± 6.11***

***Denotes very highly significant ($p<0.001$)

Table III shows that longest time for onset of induction was found in group II (Propofol 0.5%) 70.5 ± 19.58, followed by group I (Thiopentone 2.5%) 47.20 ± 7.26, where as shortest in group III (Propofol 1%) 40.1 ± 6.11.

Difference between group I and II and group I and III was statistically very highly significant ($p<0.001$).

TIME FOR ONSET OF INDUCTION IN DIFFERENT GROUPS

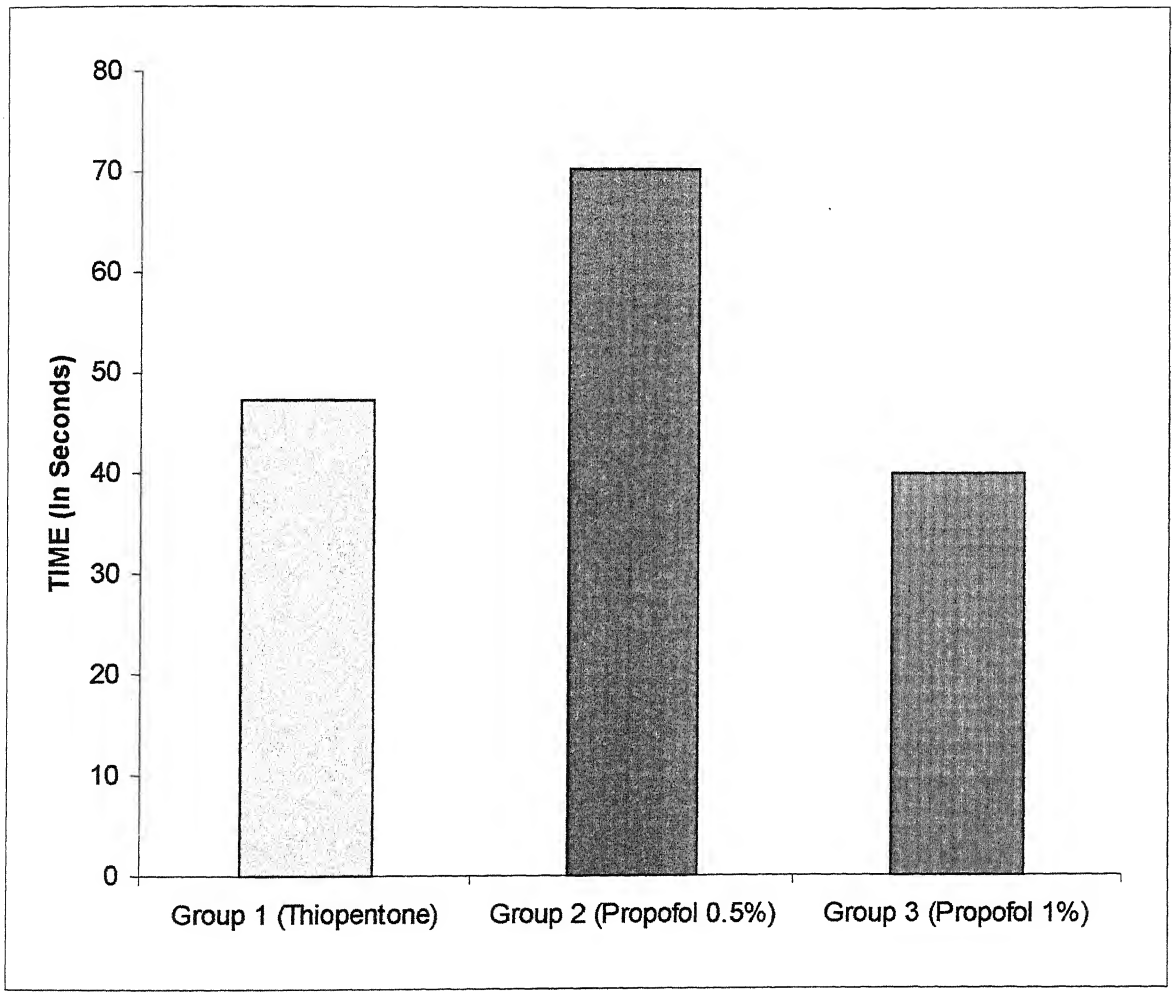


Table IV

Change Mean Pulse Rate (Mean + SD/min)

Time Interval	Group I Thiopentone (2.5%)	Group II Propofol (0.5%)	Group III Propofol (1%)
Pre - Induction	97.40 ± 13.72	103.8 ± 23.04	92 ± 17.61
During - Induction	122.4 ± 15.24***	127 ± 19.51***	107.4 ± 17.66***
During - Intubation	123.0 ± 18.67***	121.4 ± 14.04***	112.3 ± 10.41**
5 Min after Intubation	116.0 ± 13.88***	118.4 ± 12.43***	109.6 ± 13.01***
15 Min after Intubation	112.6 ± 15.65***	124 ± 14.03***	113.0 ± 14.17***
30 Min after Intubation	113.0 ± 15.76***	124 ± 12.44***	117.3 ± 14.47***
45 Min after Intubation	116.2 ± 18.85***	126.6 ± 12.67***	115.2 ± 14.95***
Just after Extubation	128.8 ± 15.09***	137 ± 17.67***	120.0 ± 22.93***
15 Min after Extubation	112.2 ± 15.89***	118.2 ± 21.20***	102.0 ± 11.89***

* - denotes significant change ($p<0.05$)

** - denotes highly significant change ($p<0.01$)

*** - denotes very highly significant change ($p<.001$)

Table shows that in all three groups there were very highly significant ($p<0.001$) rise in mean pulse rate till the end of surgery from pre-induction level.

CHANGES IN MEAN PULSE RATE

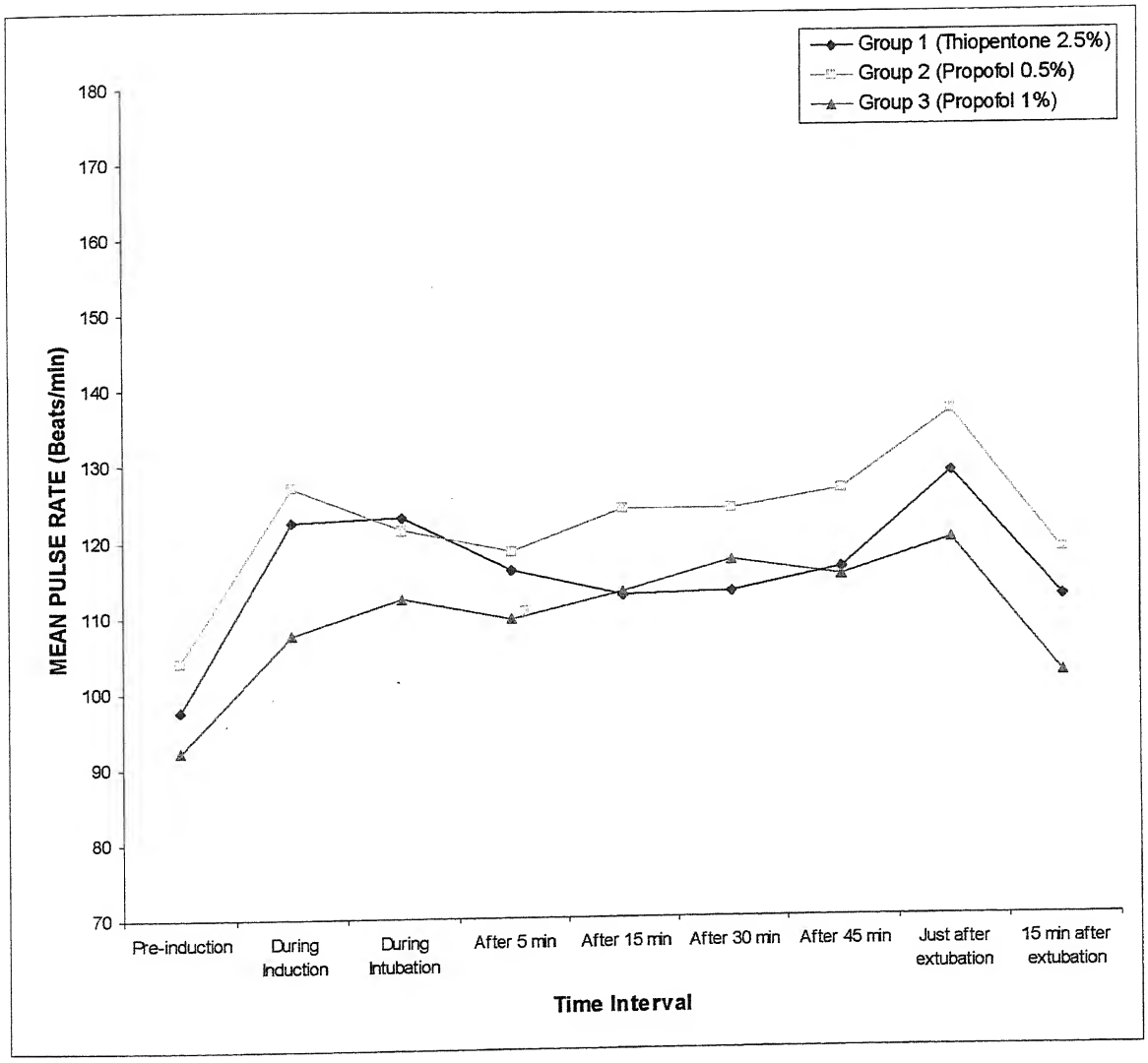


Table - V

Change in Systolic and Diastolic Blood Pressure

(Mean + SD mmHg)

Time Interval	Group I Thiopentone (2.5%)	Group II Propofol (0.5%)	Group III Propofol (1%)
Pre - Induction	122.4 ± 7.15 79.8 ± 4.93	120.2 ± 6.71 80.0 ± 5.14	122.2 ± 6.06 82.2 ± 4.67
During - Induction	118.4 ± 6.91** 76.6 ± 4.36***	120.4 ± 7.09 79.8 ± 5.33	119.2 ± 5.90** 79.2 ± 3.66***
During - Intubation	142.2 ± 7.01*** 87.2 ± 3.04***	143.8 ± 6.58*** 86.2 ± 4.40***	137.8 ± 6.65*** 86.4 ± 2.84**
5 Min after Intubation	141.4 ± 6.68*** 86.0 ± 2.22***	144.2 ± 5.92*** 86.0 ± 4.06***	122.8 ± 6.38 82.4 ± 3.72
15 Min after Intubation	124.2 ± 6.58* 81.4 ± 4.07*	141.6 ± 5.95*** 85.6 ± 4.24***	122.8 ± 6.11 81.4 ± 3.15
30 Min after Intubation	125.2 ± 6.18* 81.8 ± 4.11**	140.6 ± 4.46*** 84.4 ± 2.37**	123.2 ± 6.44 82.4 ± 4.53
45 Min after Intubation	128.2 ± 6.06*** 84.6 ± 2.73**	142.0 ± 4.89*** 84.6 ± 2.88**	122.6 ± 5.06 81.4 ± 3.86
Just after Extubation	139.8 ± 6.26*** 85.6 ± 2.54***	145.2 ± 6.88*** 87.0 ± 4.19	136.8 ± 5.69*** 85.4 ± 6.27
15 Min after Extubation	124.4 ± 7.09* 80.8 ± 3.66	121.4 ± 6.93 81.4 ± 4.90	124.0 ± 6.09** 82.8 ± 4.91

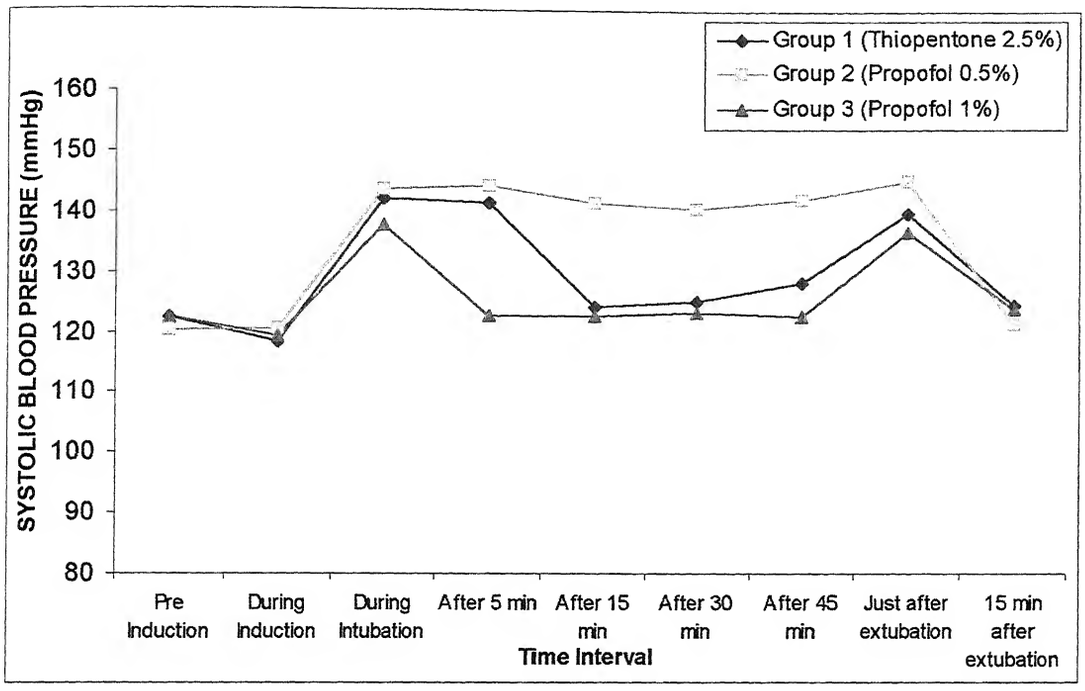
* - denotes significant change ($p<0.05$)

** - denotes highly significant change ($p<0.01$)

*** - denotes very highly significant change ($p<.001$)

Table (v) shows that there was highly significant ($p<.01$) fall in systolic blood pressure during induction, in both group I and III, and very highly significant ($p<0.001$) fall in diastolic blood pressure in group I and group III during induction. Both systolic and diastolic blood pressure rise very highly significant ($p<0.001$) during intubation in all the three groups, but in group III return of blood pressure to preoperative value 5 min after intubation, while in group I return of blood pressure after 15 min. but in group II continuous very highly significant ($p <.001$) rise in blood pressure through out the surgery.

CHANGES IN SYSTOLIC BLOOD PRESSURE



CHANGES IN DIASTOLIC BLOOD PRESSURE

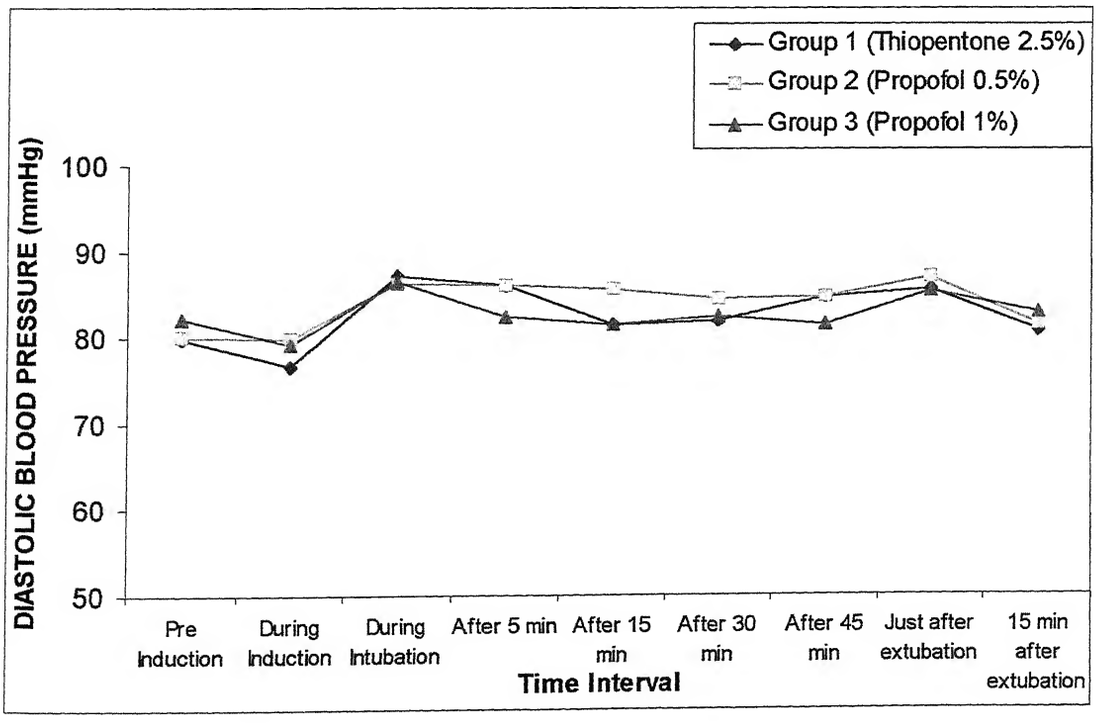


Table VI

Change in Mean Arterial Pressure

(Mean + SD mmHg)

Time Interval	Group I Thiopentone (2.5%)	Group II Propofol (0.5%)	Group III Propofol (1%)
Pre – Induction	93.99 ± 5.71	93.39 ± 5.53	94.53 ± 5.90
During – Induction	90.53 ± 5.09	93.32 ± 5.76	92.53 ± 4.24
During – Intubation	105.53 ± 3.97***	105.39 ± 4.99***	103.53 ± 3.82***
5 Min after Intubation	104.46 ± 3.55***	105.39 ± 4.64***	96.06 ± 4.78
15 Min after Intubation	95.66 ± 4.79	104.26 ± 4.60***	95.19 ± 4.08
30 Min after Intubation	96.26 ± 4.57	103.13 ± 2.91***	95.39 ± 4.92
45 Min after Intubation	98.99 ± 3.56	103.73 ± 3.42***	95.13 ± 4.12
Just after Extubation	103.66 ± 3.50***	106.19 ± 4.39***	102.52 ± 2.88***
15 Min after Extubation	95.33 ± 4.53	94.73 ± 5.30	96.52 ± 5.39

* - denotes significant change ($p<0.05$)

** - denotes highly significant change ($p<0.01$)

*** - denotes very highly significant change ($p<0.001$)

Table (VI) shows that three was very highly significant ($p<0.001$) fall in mean arterial pressure during induction in group I while insignificant ($p>0.05$) fall in group III.

In all the three groups, very highly significant ($p<0.001$) rise in mean arterial pressure during intubation were found, and early return of mean arterial pressure in group III compared to group I and II.

CHANGES IN MEAN ARTERIAL PRESSURE

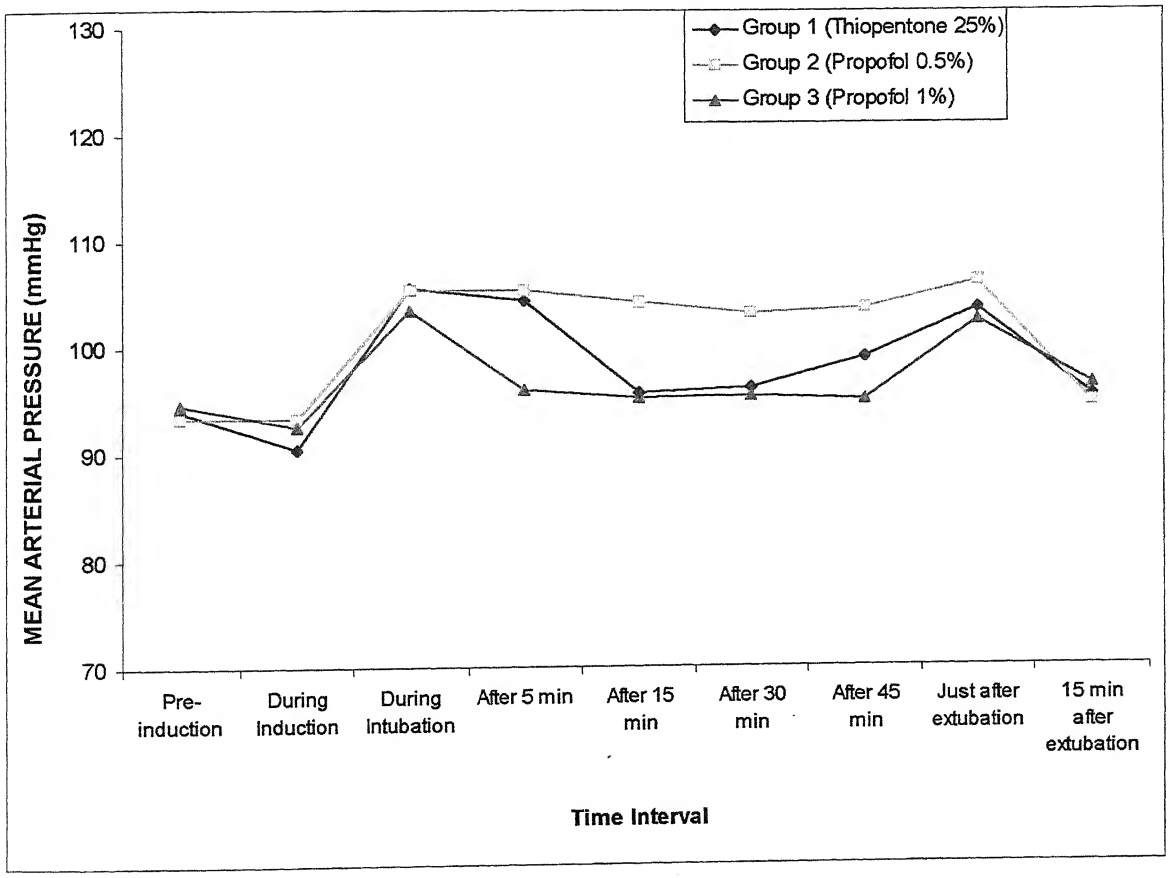


Table VII

Change in Arterial Oxygen Saturation (Mean+SD/%age)

Time Interval	Group I Thiopentone (2.5%)	Group II Propofol (0.5%)	Group III Propofol (1%)
Pre - Induction	97.8 ± 0.99	97.8 ± 0.61	97.2 ± 0.76
During - Induction	99.2 ± 0.61	99.7 ± 0.61	99.9 ± 0.30
During - Intubation	99.0 ± 0.78	99.7 ± 0.65	100.0 ± 0.00
5 Min after Intubation	98.9 ± 0.54	99.7 ± 0.65	99.9 ± 0.30
15 Min after Intubation	98.7 ± 0.46	99.7 ± 0.65	99.9 ± 0.30
30 Min after Intubation	98.7 ± 0.46	99.8 ± 0.61	99.7 ± 0.46
45 Min after Intubation	98.8 ± 0.40	99.8 ± 0.61	99.8 ± 0.40
Just after Extubation	99.4 ± 1.77	99.1 ± 0.30	99.9 ± 0.30
15 Min after Extubation	99.5 ± 0.82	98.6 ± 0.93	98.0 ± 0.64

Table (VII) shows that arterial oxygen saturation was maintained similar in all three groups.

CHANGES IN ARTERIAL OXYGEN SATURATION IN DIFFERENT GROUPS

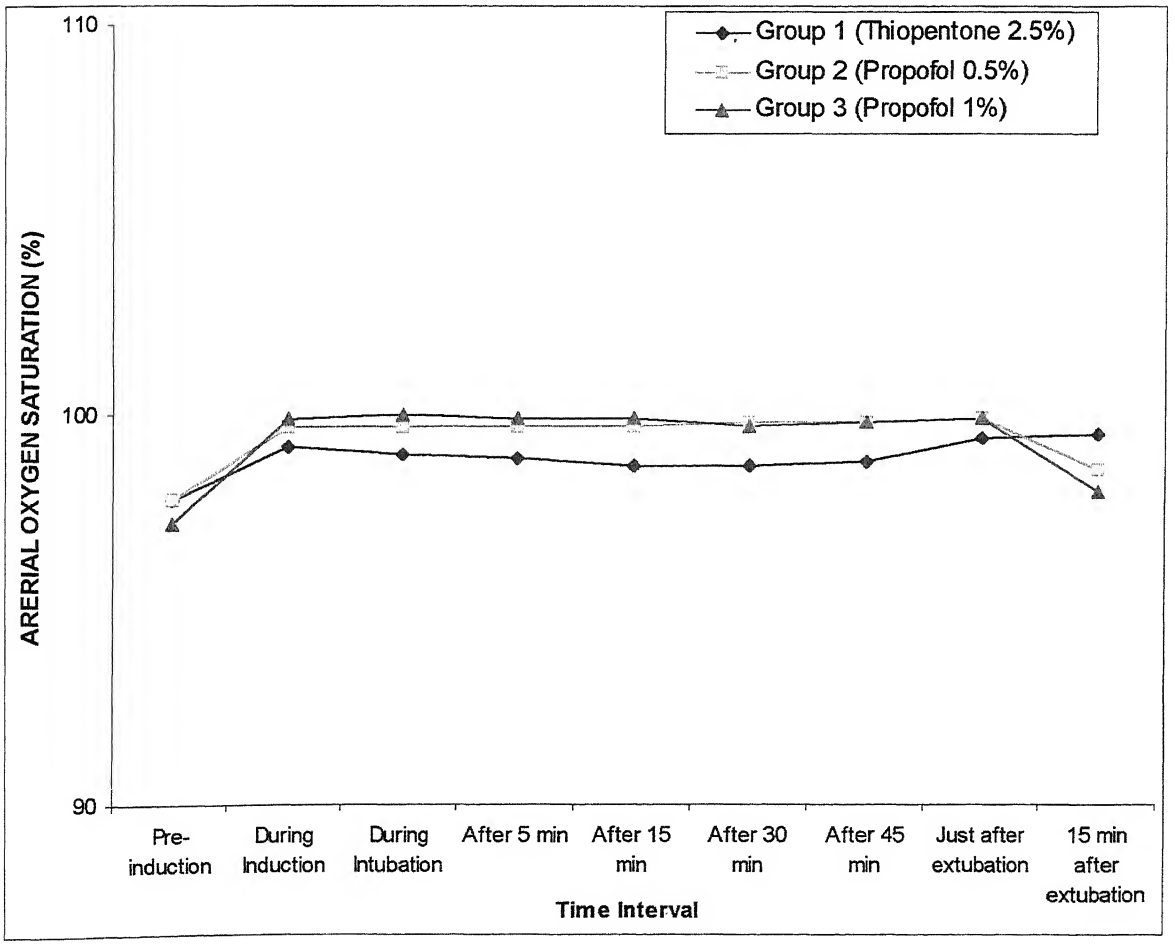


Table VIII

Changes in Induction to Delivery time (Minute)

	Group I Thipentone 2.5%	Group II Propofol 0.5%	Group III Propofol 1%
Mean ± SD	8.2 ± 1.86	8.0 ± 2.76	8.1 ± 0.71

Table (VIII) shows that there were similar time taken from induction to delivery of baby in all groups.

CHANGES IN INDUCTION TO DELIVERY TIME (MINUTES)

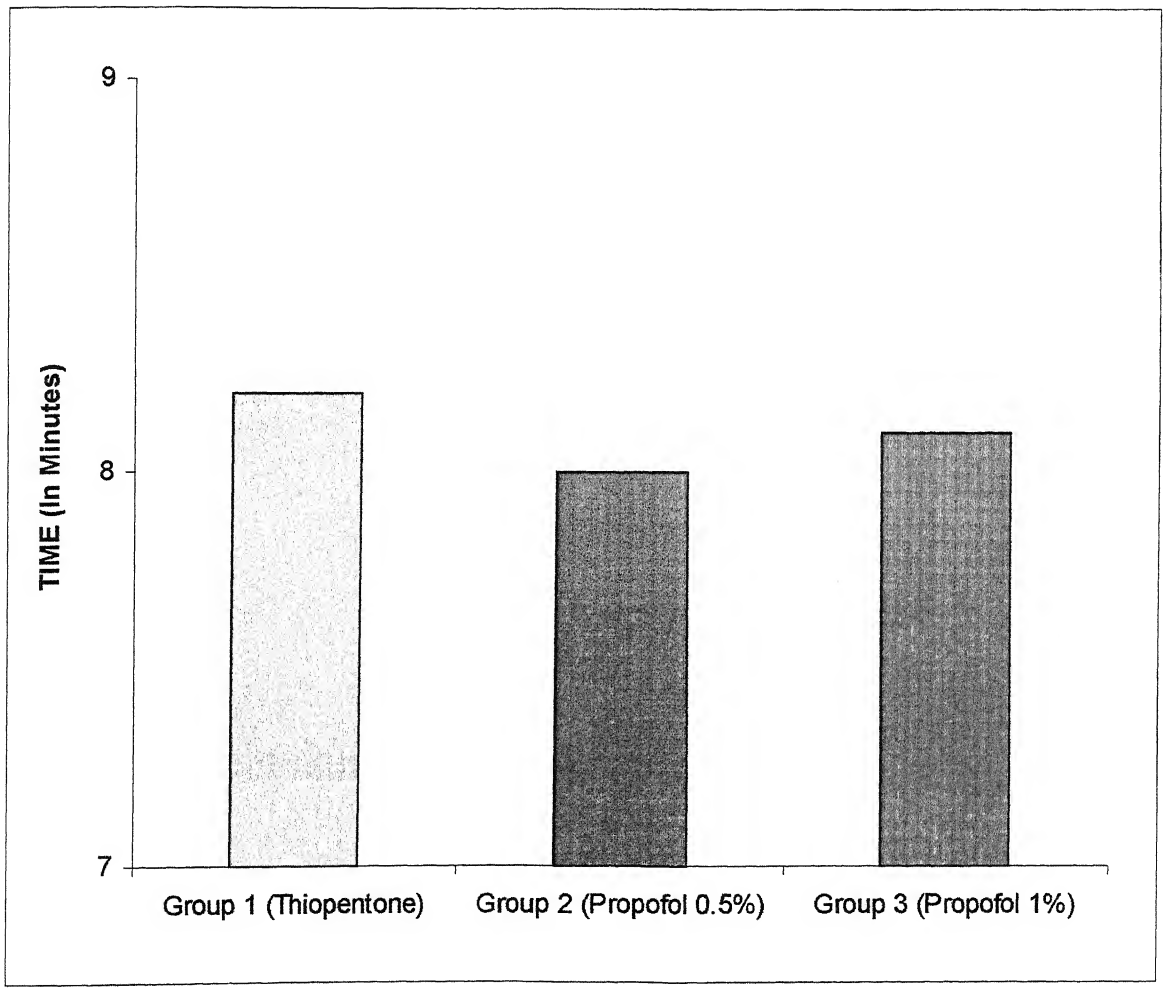


Table IX

Change in Apgar Scores

Groups		At 1 Min	At 2 Min	At 5 Min	At 10 Min	At 30 Min
Group I	Mean	6.0	7.4	8.0	9.0	9.9
Thiopentone	±	±	±	±	±	±
2.5%	SD	1.36	1.13	1.11	0.45	0.30
Group II	Mean	5.8	7.0	7.9	8.3	9.7
Propofol	±	±	±	±	±	±
0.5%	SD	0.88	0.78	0.71	1.02	0.65
Group III	Mean	6.5	7.6	8.2	9.3	9.9
Propofol	±	±	±	±	±	±
1%	SD	1.77	1.65	0.99	0.79	0.30

Table (IX) shows that lowest Apgar score at 1 min was found in group II (Propofol 0.5%) 5.8 ± 0.88, where as highest was in group III (Propofol 1%) 6.5 ± 1.77.

Difference between group I and II and group I and III was statistically insignificant ($p>0.05$).

CHANGES IN APGAR SCORES IN DIFFERENT GROUPS

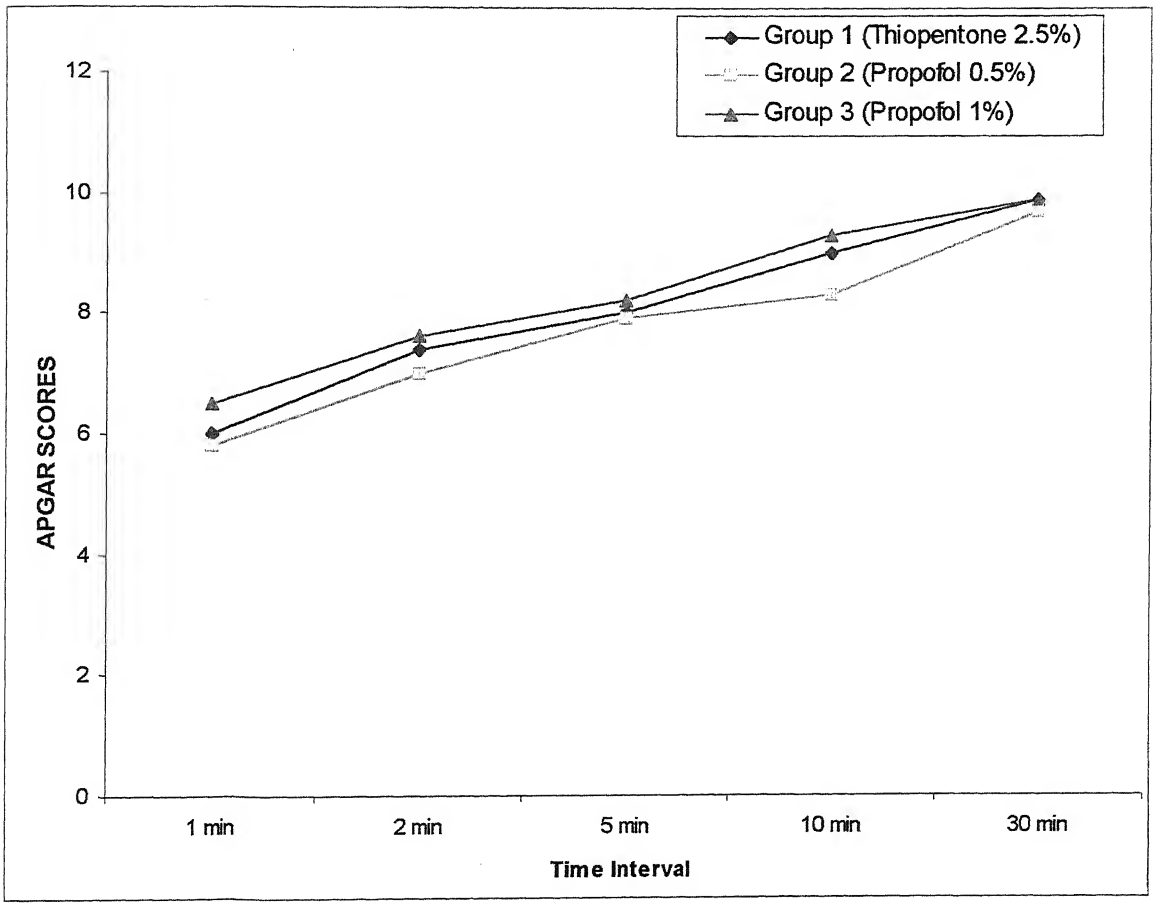


Table X

Complications

COMPLICATIONS		GROUP-I		GROUP-II		GROUP-III	
		Number	% age	Number	% age	Number	% age
1)	Pain on injection site	2	6	1	3	2	6
2)	Laryngospasm	-	-	-	-	-	-
3)	Bronchospasm	-	-	-	-	-	-
4)	Apnoea	8	26	4	13	8	26
5)	Cough	1	3	-	-	-	-
6)	Hiccup	2	6	-	-	-	-
7)	Abnormal limb Movement	-		3	10	3	10
8)	Thrombophlebitis	3	10	-	-	1	3
9)	Nausea and Vomiting	10	33	-	-	-	-
10)	Awareness introoperatively	-	-	2	6	1	3

Table (X) shows that pain on injection site was experienced by 2 patients (6%) in group I, 1 patient (3%) in group II while in group II, 2 patients (6%).

Laryngospasm and Bronchospasm were not experienced by any patient in all the three group.

Prevalence of apnoea was seen in group I and III where 8 patients (26%) each had cessation of breathing during induction while it appeared in 4 patient (13%) in group II.

Cough was experienced by 1 patient (3%) in group I while not seen in group II and III.

Hiccup was experienced by 2 patients (6%) in group I and none in group II or group III.

Abnormal limb movements were experienced by 3 patients (10%) each in group II and III while none in group I.

Post operatively prevalence of thrombophlebitis was seen in 3 patients (10%) in group I, 1 patient (3%) in group III while none in group II.

Incidence of nausea and vomiting was more in group I being in 10 patients (33%) while none in group II and III.

Awareness during surgery was found in 2 patients (6%) in group II, 1 patient (3%) in group III and not found in group I.

COMPLICATIONS IN DIFFERENT GROUPS

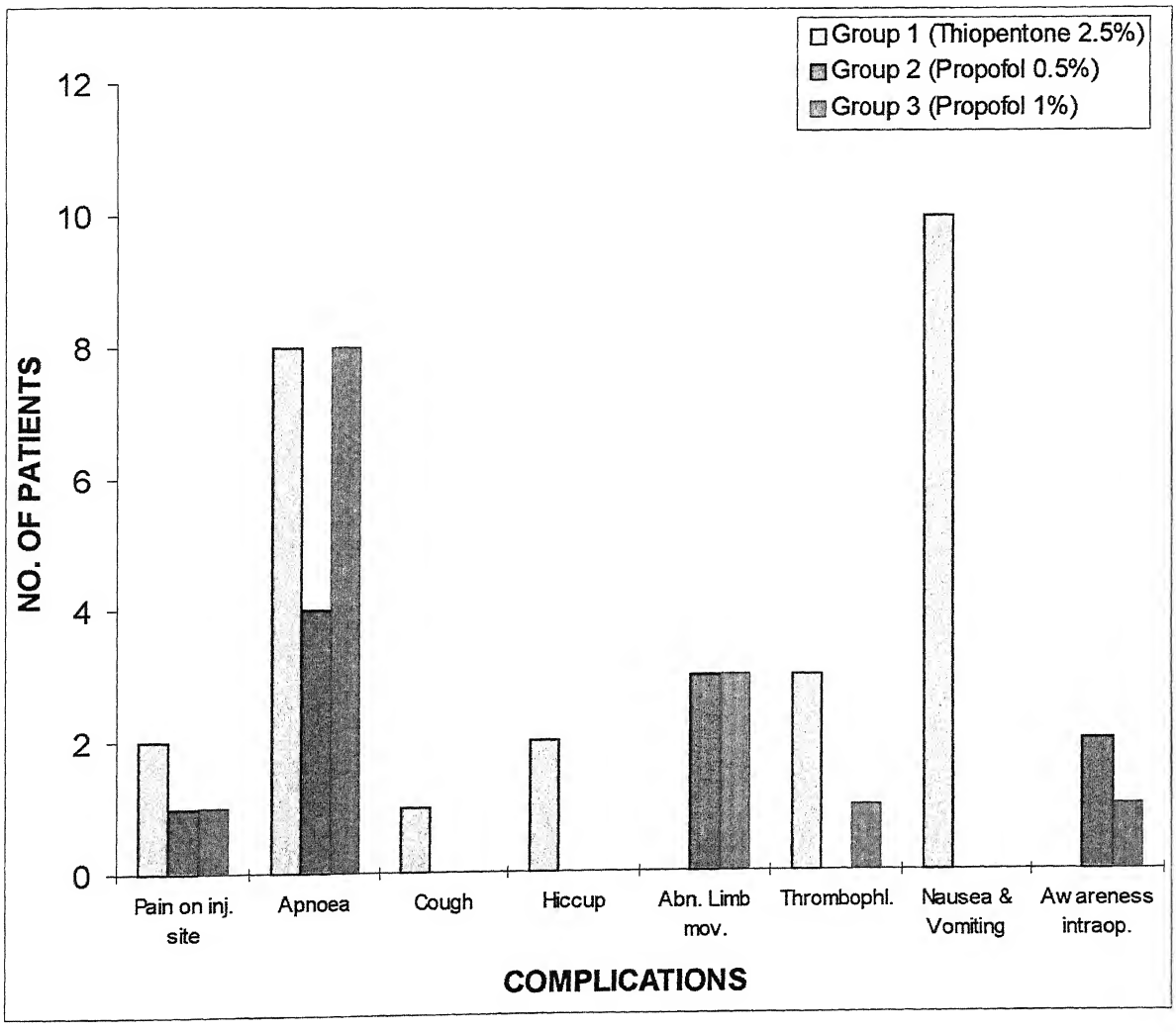


Table XI

Patients Acceptance

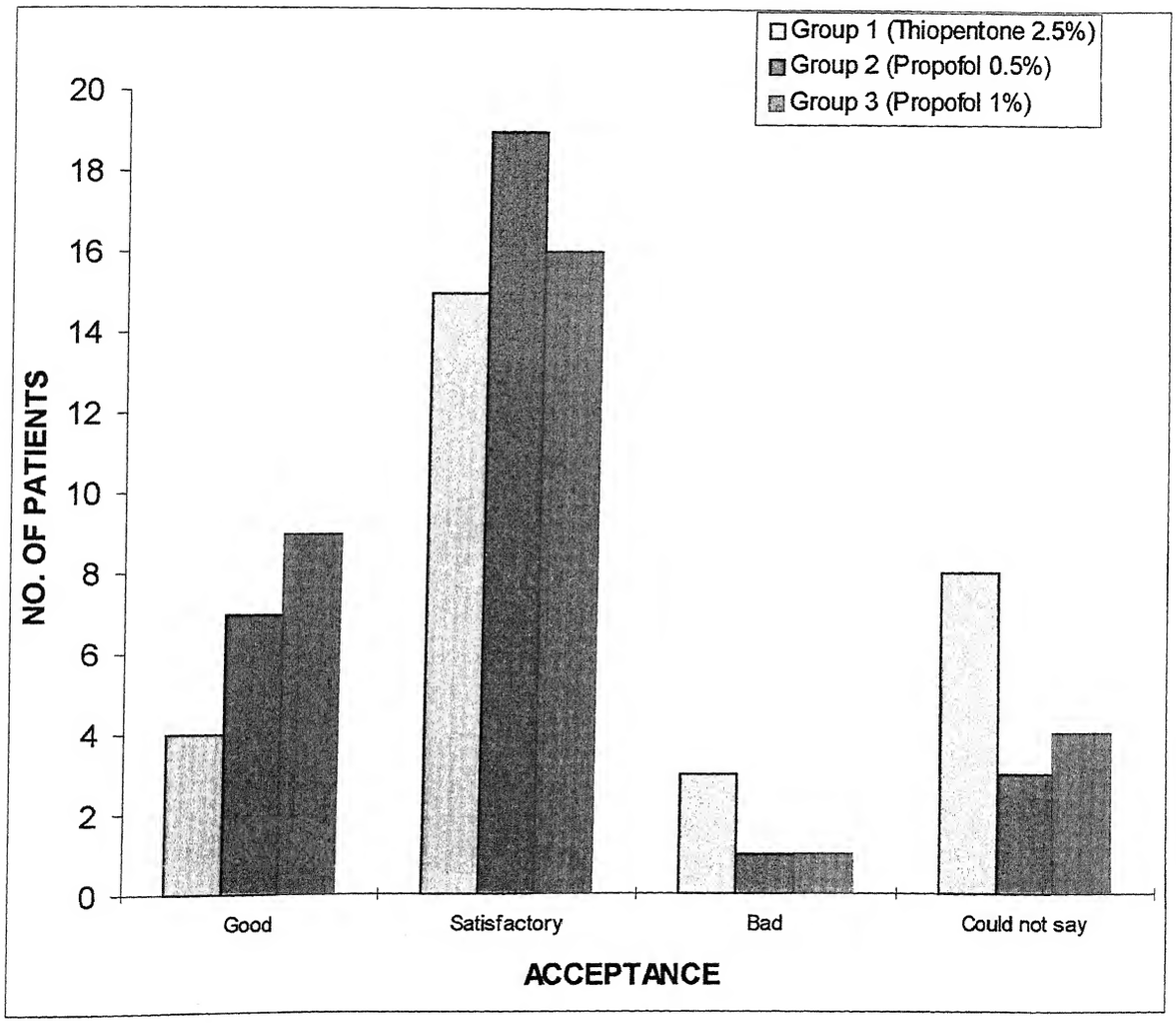
ACCEPTANCE		GROUP-I		GROUP-II		GROUP-III	
		Number	% age	Number	% age	Number	% age
1)	Good	4	13	7	23	9	30
2)	Satisfactory	15	50	19	63	16	53
3)	Bad	3	10	1	3	1	3
4)	Could not say	8	26	3	10	4	13

Table (XI) shows that induction was good in 9 patients (30%) in group III, 7, patients (23%) in group II and 4 (13%) in group I.

Induction was satisfactory in 19 patients (63%) in group II, 16 patients (53%) in group III and 15 patient (50%) in group I.

Induction was bad in 3 patients (10%) in group I and 1 patient (13%) each in group II and II. 3 patients (10%) in group II and 4 patient (13%) in group III could not say about induction.

PATIENTS ACCEPTANCE IN DIFFERENT GROUPS



DISCUSSION

DISCUSSION

The introduction of Propofol into clinical practice of intravenous anaesthesia has put yet another feather in the cap of anesthesiology. It is a remarkable success, achieved by the anesthesiologist.

Propofol allows smooth, safe and rapid induction in one-arm brain circulation time. Redistribution quickly clears it from the blood rich organ and, unlike Thiopentone it does not accumulate in the body. This allows Propofol infusions to be used to maintain anaesthesia. Less postoperative nausea and vomiting and faster emergence are charaterised by the absence of post operative confusion and sedation. Rapid recovery from anaesthesia would be advantageous in obstetric patients because of the increased risk of aspiration which may occur in the post-operative period. Seeing the foresaid advantage of Propofol it was decided to evaluate its use for induction of anaesthesia in comparison to conventional intravenous anaesthetic Thiopentone sodium for caesarean section.

The analysis of data obtained from observation made on 90 pregnant women of ASA grade I and II undergoing elective caesarean section under general anaesthesia, induced with either Thiopentone sodium 2.5% (group I)/Propofol 0.5% (group II)/Propofol 1% (group III) depicted that maximum number of patients (47.7%) belong to age group of 21–25 years (Table – I) and weighing (50%) 51 – 60 Kg (Table – II). Though age has no correlation with the selection of inducing agents.

Induction time was observed to be fastest with 1% Propofol than Thiopentone sodium and Propofol 0.5%. Mean induction time was maximum (70.5±19.58 seconds) in group II, minimum (40.1±6.11 seconds) in group III and in between (47.2±7.26 seconds) in group I (Table III). Our finding of rapid induction with Propofol is in conformity with Kotur P.F. et al (2000).

Thiopentone Sodium and Propofol exert their action through GABA receptors. Thiopentone Sodium and Propofol being highly lipophilic in nature rapidly crosses the blood brain barrier thus accounting for their rapid onset of action.

The doses used for induction was fixed according to body weight which was adequate to reach the induction criteria i.e. loss of eyelid reflex in group I (5 mg/kg body weight) and II and III (2 mg/kg body weight). No patients required additional doses for induction of anaesthesia. Doses used by Gint T. et al (1990), Celleno D, et al (1989) were almost similar.

In present study there was a highly significant ($p < 0.01$) increase in mean pulse rate from preinduction values at induction, during intubation, 5 min, 15 min, 30 min and 45 min after intubations (Table IV). Thus confirming the views of Valtonen M. et al (1989), Siafaka et al (1992) and Kotur P.F. et al (2000), who found a similar rise in mean pulse rate in all the groups.

Since Thiopentone produces peripheral vasodilatation causing pooling of blood in the extremities and reduction in the venous return to the heart

leading thereby to decrease in cardiac output. There is some degree of tachycardia (10%-20%), which with lower doses contribute to maintenance of the blood pressure and cardiac output. Higher doses causes increasing myocardial depression and vasodilation but tolerable with normal cardiovascular system.

Propofol decreases the arterial blood pressure during induction of anaesthesia. An induction dose of 2 to 2.5mg/kg produces a 25 – 40 percent reduction of systolic blood pressure. Similar changes are seen in mean and diastolic blood pressure. The decrease in arterial pressure is associated with a decrease in cardiac output/cardiac index (≈15%), stroke volume index (≈20%) and systemic vascular resistance (15 – 25%), left ventricular stroke work index is also decreased (≈30%). Heart rate does not change significantly after an induction dose of Propofol because it either resets or inhibit the baroreflex, thus reducing the tachycardic response to hypo tension.

In all the groups show rising tendency in blood pressure (systolic and diastolic) particularly at intubation varied significant to highly significant. In group III there is early return of blood pressure to pre-operative level at 5 min after intubations, in group I return of blood pressure at 15 minute after intubation's while in group II blood pressure was raised throughout the surgery.

Moore J. et al (1989) found that haemodynamic response to Propofol and thiopentone were similar. Gin T. et al (1990) concluded that post induction arterial pressures were similar to pre-induction values with no

differences. Following intubation, the rise in systolic arterial pressure was greater in the Thiopentone group. In the Thiopentone group, arterial pressure were slower in returning to baseline values.

Yau G. et al (1991) found that hypertensive response after intubation was of shorter duration in the Propofol group compared with Thiopentone group. Djordjevic B. et al (1998) concluded that following induction of anaesthesia a significantly greater decrease of blood pressure was found in the Propofol group, when compared with the patients in Thiopentone group.

All the patients were preoxygenated for 3 to 5 minutes with 100% oxygen which was continued during induction and with onset of apnoea, patients were ventilated manually with 100% oxygen. After intubation, patients were maintained on N_2O and O_2 (60% and 40% respectively), there fore arterial oxygen saturation was maintained similar in all three groups.

Apgar scores were found 8 at 5 minutes in all three groups, although lowest Apgar score at 1 minute was found in group II (5.8 ± 0.88), where as highest was in group I (6.5 ± 1.77), but difference between group I and II, and group I and III was statistically insignificant. Our finding is in conformity with Kanto J. et al (1990) concluded that on the basis of Apgar scores and blood gas analyses of the feto-placental unit, Propofol appears to be a safe alternative to other available induction agents. Siafaka I. et al (1992) found that there was no significant neonatal depression as assessed by Apgar scores and blood gas analyses. Gin T. et al (1993) concluded that neonatal apgar scores, neurobehavioural testing and umbilical catecholamine, blood gas tension and oxygen content analysis were similar between Propofol and Thiopentone groups. Zamora E. et al (1994) studied

the effects on the new born infant of thiopental and Propofol used in anaesthetic induction in caesarean section, he concluded that if the induction-extraction interval is 10 minutes or less, both thiopental and Propofol given in a single dose for induction of general anaesthesia in all types of caesarean section are equally safe for the new born infant.

Pain on injection was experienced by 2 patients (6%) each in group I and III, and 1 patient (3%) in group II. Thrombophlebitis had occured in 3 patients (10%) in group I, 1 patient (3%) in group III and none in group II. These complications in group I are due to alkaline nature of solution and more frequent when small veins are used for induction. Abonormal limb movements are seen in 3 patients (10%) each in group II and group III.

Apnoea had occured in all 3 groups but maximum 8 patients (26%) each in group I and III, and minimum 4 patients (13%) in group II. Propofol affects the respiratory system in a manner qualitatively similar to the action of Thiopentone. Taylor M.B. et al (1986) and Goodman N.W. et al (1987) confirmed this result. Apnoea after an induction dose of Propofol : The incidence and duration of apnoea appear to be dependent on dose and speed of injection. An induction dose of Propofol results in a 25 to 30 percent incidence of apnoea. This was concluded by Sanderson J.H. et al (1988) and Taylor M.B. et al (1986).

Cough was experienced by 1 patient (3%) and hiccup by 2 patients (6%) in group I, while none of these complication in group II and III. Higher incidence of cough and hiccup in Thiopentone group is due to heightening of laryngeal reflexes. Barker P. et al (1992) suggested that laryngeal reflexes are more active after induction with thiopental than with equivalent doses of Propofol.

Nausea and vomiting was found in 10 patients (33%) in group I, none in group II and III. Absence of nausea and vomiting in Propofol group is confirmatory to finding of Mc Collum U.S.C. et al (1988), who concluded that Propofol posses significant antiemetic activity at low doses. Propofol has been used successfully to treat post operative nausea in a bolus dose of 10 mg by Borgeat A. et. al (1992).

Awareness intra-operatively was found in 2 patient (6%) in group II and in 1 patient (3%) in group III, and not found in group I. In conformity of it Kelly J.S. et al (1992), who concluded that awareness during surgery at higher infusion rate has been found. Celleno D.et al (1993) concluded that electroencephalographic patterns showed a light depth of anaesthesia with Propofol and midazolam between anaesthesia induction and delivery as compared to Thiopentone sodium, confirmed by the presence of clinical sign of light anaesthesia in 50% of Propofol patient and 43% of midazolam patient.

Acceptance of induction phase was good in 4 patients (13%), satisfactory in 15 patients (50%) and 3 patient (10%) complained about bad experience during induction and 8 patients (26%) could not say in group I. This comparison of acceptance of induction is entirely subjective.

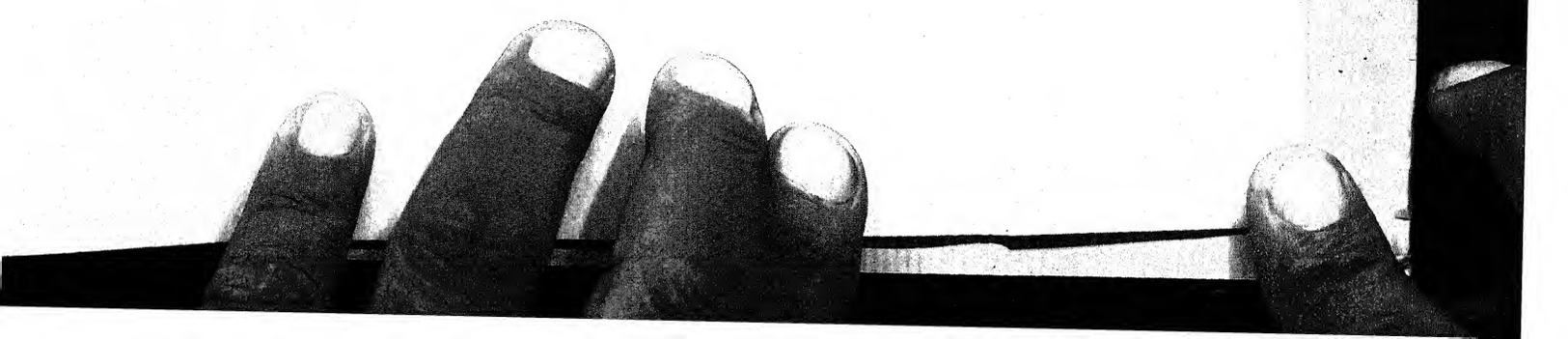
In group II, acceptance of induction phase was good in 7 patients (23%) satisfactory in 19 patients (63%), bad in 1 patient (3%) and 3 patients (10%) could not tell.

Acceptance was good in 9 patients (30%) in group III, satisfactory in 16 patients (53%), bad in 1 patient (3%) and 4 patient (13%) could not tell.

Compared to patients of group II and III, patients of group I remains sedated for prolonged period after surgery although they are arousable.

Thus it appear that Propofol is as good as Thiopentone as an induction agent for obstetric anaesthesia in the sense that it preserves materno-foetal well being. It appears to have an edge over the later drug by producing rapid and clear headed recovery and absence of nausea vomiting. Thus minimizing the chances of post operative aspiration pneumonitis.

CONCLUSION



CONCLUSION

On completion of the study and analysis of the data obtained, following conclusion was derived at:

1) The induction time was found to be shortest with Propofol 1% (40.1 ± 6.11 seconds) as compared to Thiopentone 2.5% (47.2 ± 7.26 seconds) and Propofol 0.5% (70.5 ± 19.58 seconds).

2) Induction was smooth with both Propofol (0.5 or 1%) and Thiopentone (2.5%).

3) Stability of pulse and blood pressure with Thiopentone (2.5%) and Propofol (1%) induction were comparable and better than Propofol 0.5% induction.

4) Maintenance of arterial oxygen saturation was good with all three agents.

5) Incidence of respiratory depression was similar with Propofol 1% in comparison to Thiopentone sodium 2.5%, less with Propofol 0.5%.

6) Apgar scores at 1,2,5,10 and 30 minutes were comparable between all groups, was more with Propofol 1% than with Propofol 0.5% and Thiopentone sodium 2.5%.

7) Incidence of complications like

   (a) Pain on injection were similar with Propofol 1% and Thiopentone 2.5% while less with Propofol 0.5%.

(b) Thrombophlebitis occurred more with Thiopentone than with Propofol 0.5% and 1%

(c) Abnormal limb movements were found only with Propofol 0.5% and 1%, not with Thiopentone group.

(d) Cough and hiccup were found only with Thiopentone not with Propofol 0.5 or 1%.

(e) Apnoea had occurred equally with Propofol 1% and Thiopentone sodium 2.5% but less with Propofol 0.5%.

8) Incidence of nausea and vomiting was nil with Propofol 0.5% and 1%, while 33% with Thiopentone sodium 2.5%.

9) Incidence of awareness during induction was found more in Propofol 0.5% (6%) than Propofol 1% and Thiopentone sodium 2.5%.

10) The over all acceptance of induction was higher with Propofol 1% than with Propofol 0.5% and Thiopentone sodium 2.5%.

Thus it was concluded that Propofol 1% is an effective, safe and reasonable atternative to Thiopentone sodium 2.5% as an induction agent for general anesthesia for caesarean section.

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SUMMARY

The present study was conducted on 90 young pregnant patients of ASA grade I and II, in the age from 18 to 35 years admitted in the department of Gynaecology and obstetrics M.L.B. Medical college and hospital Jhansi scheduled for elective caesarean section under general anaesthesia. Each selected patient was randomly assigned to one of the three following group containing 30 patients each and depending on the induction agent used

Group I - Thiopentone sodium 2.5% (5 mg/kg body weight)

Group II - Propofol 0.5% (2 mg/kg body weight)

Group III - Propofol 1% (2 mg/kg body weight)

Patients were subjected to a thorough pre-anaesthetic checkup including detailed clinical history and clinical examination Required investigations were done. All patients were assured and reassured during pre-anaesthetic checkup. Proposed technique of anaesthesia was explained to every one and an informed and written consent was in detail taken. Premedication was done with injection Metoclopramide (0.2 mg/kg body weight) and injection Ranitidine (1.0 mg/kg body weight) intramuscularly, 45 minutes before induction of anaesthesia. Injection Atropine (15 µg/kg body weight) was given intravenously 5 minutes before induction of anaesthesia inside the operation theatre through an I/V line preset using 5% Dextrose solution. Preoxygenation was done with 100% oxygen for 3-5 minutes Patient were induced by either Thiopentone sodium

5 mg kg body weight (Group – I) or Propofol 2 mg/kg body weight 0.5% solution (Group II) or Propofol 1% (Group III) through slow I/V injection over a period of 30 seconds. Ventilation was assisted with 100% of oxygen as and when apnoea occurred. Laryngoscopy was then performed under the effect of suxamethonium in doses of 1.5 mg kg-1 body weight and proper size endotracheal tube introduced atraumatically. Patients were then connected to Boyle's Basic Anaesthetic machine via Bain's rebreathing anaesthetic circuit and I.P.P.V started.

Anaesthesia was maintained with O2 and N2O in a ratio of 40:60 and vecuronium bromide and intermittent positive pressure ventilation On completion of surgery residual neuromuscular block was reversed by neostigmine (45 µg/kg body weight) and Atropine (25 µg/kg body weight) I/V slowly.

During induction following data were observed and recorded :

1) Pain on injection

2) Induction time in seconds from injection to spontaneous closure or loss of eyelid reflex

3) Pulse rate
4) Blood pressure – Systolic and diastolic
5) Arterial oxygen saturation

} During induction during intubation and then at regular interval till the end of surgery.

6) Abnormal limb movements

7) Presence or absence of apnoea

8) Side effects if any like cough and hiccup

9) Apgar scores

10) Post operatively patients were enquired about acceptance with particular reference to induction phase and any incidence of awareness during anaesthesia.

On completion of the study and analysis of the data obtained, following conclusion was derived at:

1) The induction time was found to be shortest with Propofol 1% (40.1 $\pm$ 6.11 seconds) as compared to Thiopentone 2.5% (47.2 $\pm$ 7.26 seconds) and Propofol 0.5% (70.5 $\pm$ 19.58 seconds).

2) Induction was smooth with both Propofol (0.5 or 1%) and Thiopentone (2.5%).

3) Stability of pulse and blood pressure with Thiopentone (2.5%) and Propofol (1%) induction were comparable and better than Propofol 0.5% induction.

4) Maintenance of arterial oxygen saturation was good with all three agents.

5) Incidence of respiratory depression was similar with Propofol 1% in comparison to Thiopentone sodium 2.5%, less with Propofol 0.5%.

6) Apgar scores at 1,2,5,10 and 30 minutes were comparable between all groups was more with Propofol 1% than with Propofol 0.5% and Thiopentone sodium 2.5%.

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   (a) Pain on injection were similar with Propofol 1% and Thiopentone 2.5% while less with Propofol 0.5%.

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10) The over all acceptance of induction was higher with Propofol 1% than with Propofol 0.5% and Thiopentone sodium 2.5%.

Thus it appears that Propofol is as good as Thiopentone as an induction agent for obstetric anaesthesia in the sense that it preserves materno-foetal well being. It appears to have an edge over the later drug by producing rapid and clear headed recovery and absence of nausea and vomiting thus minimizing the chance of post-operative aspiration pneumonitis.